Proposed Registration Decision PRD2014-25

Trichoderma harzianum strain T-22

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Overview

Proposed Registration Decision for *Trichoderma harzianum* strain T-22

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Trianum Technical (containing the active ingredient *Trichoderma harzianum* strain T-22), Trianum WG Biological Fungicide and Trianum G Biological Fungicide for the suppression of soil-borne pathogens that cause root diseases on greenhouse crops, field crops, greenhouse ornamentals and turf.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Trianum Technical, Trianum WG Biological Fungicide and Trianum G Biological Fungicide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act.*

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

Before making a final registration decision on *Trichoderma harzianum* strain T-22, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on *T. harzianum* strain T-22, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is *Trichoderma harzianum* strain T-22?

T. harzianum strain T-22 is a fungus that protects plants from disease-causing fungal pathogen. *T. harzianum* strain T22 is a beneficial fungus that out competes plant pathogenic fungi for space and nutrients, colonizing the plant roots ahead of the pathogens. It also acts as a mycoparasite by producing enzymes which break down the hyphae of the plant pathogenic fungi. The mechanisms of biocontrol with *T. harzianum* are complex and generally considered in competition with plant pathogens for space and substrates in the rhizosphere, mycoparasitism and the secretion of cell wall degrading enzymes, production of antifungal substances, and induction of systemic resistance.

Trianum WG Biological Fungicide and Trianum G Biological Fungicide are end-use products that are proposed for use as commercial-class biological fungicides to suppress various root diseases caused by *Rhizoctonia solani*, *Fusarium oxysporum*, *Pythium ultimum*, *P. aphanidermatum*, *P. violae* on greenhouse crops, field crops and greenhouse ornamentals as well as reducing symptoms of dollar spot (*Sclerotinia homoeocarpa*) and microdochium patch (*Microdochium nivale*) on turf. Trianum WG Biological Fungicide is applied as a suspension, while Trianum G Biological Fungicide is mixed directly into the substrate.

Health Considerations

Can Approved Uses of *T. harzianum* strain T-22 Affect Human Health?

***T. harzianum* strain T-22 is unlikely to affect your health when Trianum WG Biological Fungicide and Trianum G Biological Fungicide are used according to the label directions.**

People could be exposed to *T. harzianum* strain T-22 when handling and applying Trianum WG Biological Fungicide and Trianum G Biological Fungicide, and when ingesting treated produce. When assessing health risks, several key factors are considered:

- the microorganism's biological properties (for example, production of toxic by-products);
- reports of any adverse incidents;
- its potential to cause disease or toxicity as determined in toxicological studies; and

[3] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.
[4] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

- the level to which people may be exposed relative to exposures already encountered in nature to other isolates of this microorganism.

Toxicological studies in laboratory animals describe potential health effects from large doses in order to identify any potential pathogenicity, infectivity and toxicity concerns. When Trianum Technical, Trianum WG Biological Fungicide and Trianum G Biological Fungicide were tested on laboratory animals, there were no signs that it caused any significant toxicity or disease.

Residues in Water and Food

Dietary risks from food and water are not of concern.

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine whether the consumption of the maximum amount of residues, that are expected to remain on food products when a pesticide is used according to label directions, will not be a concern to human health. This maximum amount of residues expected is then legally established as a maximum residue limit (MRL) under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act*. Health Canada sets science-based MRLs to ensure that the food Canadians eat is safe.

When *T. harzianum* strain T-22 was administered orally to rats, no signs that it caused toxicity or disease were observed. Secondary metabolites of toxicological significance (in other words, peptaibols) have been shown to be produced by certain naturally occurring strains of *T. harzianum* (including strain T-22). However, the use of Trianum WG Biological Fungicide and Trianum G Biological Fungicide is not expected to result in a sustained increase in levels of these peptaibols beyond the naturally occurring background levels of those produced by native *T. harzianum* strains. These metabolites are expected to be short lived in the environment once produced, as they are susceptible to ultraviolet light, high temperatures and various microbial processes in the environment. Therefore the establishment of a MRL is not required for *T. harzianum* strain T-22. As well, the likelihood of residues contaminating drinking water supplies is negligible to non-existent. Consequently, dietary risks are minimal to non-existent.

Risks in Residential and Other Non-Occupational Environments

Estimated risk for non-occupational exposure is not of concern.

Trianum WG Biological Fungicide and Trianum G Biological Fungicide are proposed for use on agricultural crops, ornamentals and turf. Consequently, adults, youths and toddlers may be exposed to *T. harzianum* strain T-22 through contact on treated turf. However, risks to the general population are not of a concern since there were no signs of disease or toxicity noted in toxicological studies with Trianum Technical, Trianum WG Biological Fungicide and Trianum G Biological Fungicide.

Occupational Risks From Handling Trianum WG Biological Fungicide and Trianum G Biological Fungicide

Occupational risks are not of concern when Trianum WG Biological Fungicide and Trianum G Biological Fungicide are used according to label directions, which include protective measures

Workers handling Trianum WG Biological Fungicide and Trianum G Biological Fungicide can come into direct contact with *T. harzianum* strain T-22 on the skin, in the eyes or by inhalation. For this reason, the product label will specify that workers exposed to the end-use products must wear waterproof gloves, long-sleeved shirts, long pants, a dust/mist filtering respirator/mask (NIOSH approval number prefix TC-21) or NIOSH approved respirators (with any N-95, P-95, R-95 or HE filter), and shoes plus socks. Eye goggles are not required as the eye irritation studies submitted indicated minimal eye irritation potential.

For the bystander, exposure is expected to be much less than that of handlers and mixer/loaders and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When *Trichoderma harzianum* strain T-22 Is Introduced Into the Environment?

Environmental risks are not of concern

T. harzianum is commonly isolated from terrestrial environments and is part of the soil micro-flora. Information available in the published literature on the environmental fate of *T. harzianum* strain T-22 suggests that, as a soil microorganism, it is likely to survive in outdoor soil under suitable environmental conditions, in other words, survival depends on the type of soil, moisture, acidity levels and temperature. Over time, however, the populations of *T. harzianum* strain T-22 should return to naturally occurring levels.

Trianum G Biological Fungicide and Trianum WG Biological Fungicide are not intended for aquatic uses and exposure to aquatic environments is limited to spray drift and run-off (following a rain event) from field applications. *T. harzianum* is not an aquatic species and is not likely to survive in aquatic environments.

Studies were conducted to determine the effects of *T. harzianum* strain T-22 on birds and bees. These studies showed that the technical grade active ingredient was not toxic or pathogenic to birds and bees.

Although non-target testing was not conducted on wild mammals, fish, some beneficial insects, microorganisms and plants, adequate information was available to determine that no significant adverse effects to these non-target organisms are expected.

Value Considerations

What Is the Value of Trianum WG Biological Fungicide and Trianum G Biological Fungicide?

Trianum WG Biological Fungicide and Trianum G Biological Fungicide, both containing *Trichoderma harzianum* strain T-22, are used preventatively for the suppression of soil-borne pathogens that cause root diseases.

Trianum WG Biological Fungicide and Trianum G Biological Fungicide are applied to soil in solution or mixed directly to the substrate, respectively. Trianum WG Biological Fungicide and Trianum G Biological Fungicide contribute to the suppression and management of plant diseases that might otherwise require applications of conventional fungicides for disease control. The use of Trianum WG Biological Fungicide and Trianum G Biological Fungicide may help reduce conventional fungicide use in greenhouses and the field.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the labels of Trianum Technical, Trianum WG Biological Fungicide and Trianum G Biological Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

In individuals exposed repeatedly to potentially large quantities of Trianum WG Biological Fungicide and Trianum G Biological Fungicide respiratory and dermal sensitivity may possibly develop. All microorganisms, including *T. harzianum* strain T-22, contain substances that are potential sensitizers. Therefore, anyone handling or applying these products must wear appropriate waterproof gloves, a long-sleeved shirt, long pants, a dust/mist filtering respirator/mask (NIOSH approval number prefix TC-21) or NIOSH approved respirators (with any N-95, P-95, R-95 or HE filter), and shoes plus socks. In enclosed areas including greenhouses, all unprotected workers are restricted from entering areas where Trianum WG Biological Fungicide and Trianum G Biological Fungicide have been handled or applied to soil until dusts have settled.

Environment

The end-use product label will include environmental precaution statements that prevent the contamination of aquatic systems from the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide.

Next Steps

Before making a final registration decision on *T. harzianum* strain T-22, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on *Trichoderma harzianum* strain T-22 (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Trichoderma harzianum strain T-22

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active ingredient	Live spores of *Trichoderma harzianum* strain T-22
Function	Biological Fungicide – To suppress various root diseases caused by *Rhizoctonia solani*, *Fusarium oxysporum*, *Pythium ultimum*, *P. aphanidermatum*, *P. violae* on greenhouse crops, field crops and greenhouse ornamentals as well as reducing symptoms of dollar spot (*Sclerotinia homoeocarpa*) and microdochium patch (*Microdochium nivale*) on turf
Binomial name	*T. harzianum* Rifai strain T-22
Taxonomic designation[1]	
Kingdom	Fungi
Subkingdom	Dikarya
Phylum	Ascomycota
Subphylum	Pezizomycotina
Class	Sordariomycetes
Subclass	Hypocreomycitidae
Order	Hypocreales
Family	Hypocreaceae
Genus	*Trichoderma*
Species	*harzianum*
Strain	T-22
Patent Status information	None.
Nominal purity of active	Technical Grade Active Ingredient: 58.99% w/w *T. harzianum* strain T-22, $>3\times10^9$ spores per gram. End-Use Products: Trianum G Biological Fungicide contains 0.32% w/w *T. harzianum* strain T-22, 1.5×10^8 CFU per gram; Trianum WG Biological Fungicide contains 3.65% w/w *T. harzianum* strain T-22, 1×10^9 CFU per gram
Identity of relevant impurities of toxicological, environmental and/or significance.	The technical grade active ingredient does not contain any impurities or micro contaminants known to be Toxic Substances Management Policy (TSMP) Track 1 substances. The product must meet microbiological contaminants release standards. Trianum end-use products may contain antibiotic peptides collectively known as peptaibols. The absence of toxic effects in mammalian acute toxicity studies (see Section 3.1.1) suggests that the manufacturing process either does not favour the production of these potentially toxic metabolites or that the levels produced are too low to elicit an effect in animals administered a high dose of this fungus.

[1] Based on *Hypocrea lixii* (teleomorph), http://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi

1.2 Physical and Chemical Properties of the Technical Grade Active Ingredient and the End-Use Products

Technical Grade Active Ingredient – Trianum Technical

Property	Result
Colour	dark green
Physical State	liquid at 22.6°C
Odour	earthy (mushroom-like) odour
Stability	stable after 7 weeks of storage in a deep-freezer at -18°C
Corrosion Characteristics	no corrosion, leakage, or other undesired effects were observed
pH	pH undiluted solution: 5.79 at 22.5°C pH 1% diluted suspension: 6.13 at 22.7°C
Viscosity	150 cP
Density	1.20 g/mL

End-Use Product – Trianum G Biological Fungicide

Property	Result
Colour	RAL 8000 brown green (no modifications after 6 months at 4–8°C)
Physical State	Granular
Odour	earthy odour (no modifications after 6 months at 4–8°C)
Stability	stable after 6 months of storage at 4–8°C
Corrosion Characteristics	no evidence of corrosion was observed
pH	Initial: pH 1% aqueous suspension: 6.64 at 22°C After 6 months at 4–8°C: pH 1% aqueous suspension: 6.21 at 24°C
Density	0.593 g/mL pour density 0.642 g/mL tap density
Particle Size Distribution	Initial: $x \geq 850$ µm =0.07% 850 µm > $x \geq 710$ µm ≥= 0.48% 710 µm > $x \geq 500$ µm ≥ =22.38% 500 µm > $x \geq 425$ µm =35.69% 425 µm > $x \geq 355$ µm =23.16% 355 µm > $x \geq 250$ µm =17.10% 250 µm > $x \geq 0$ µm =1.11% After 6 months at 4–8°C: $x \geq 850$ µm =0.05%

Property	Result
	850 µm > x ≥ 710 µm ≥= 0.73% 710 µm > x ≥ 500 µm ≥ =17.76% 500 µm > x ≥ 425 µm =34.46% 425 µm > x ≥ 355 µm =24.74% 355 µm > x ≥ 250 µm =19.72% 250 µm > x ≥ 0 µm =2.55%
Dust Content	Initial: 0.015% Nearly dust-free (4.5 mg) After 6 months at 4–8°C: 0.022%, Nearly dust-free (6.5 mg)
Friability and Attrition	Initial: Friability and attrition resistance 99.95% After 6 months at 4–8°C: Friability and attrition resistance 99.94%
Flowability	The sample flows naturally through the sieve.

End-Use Product – Trianum WG Biological Fungicide

Property	Result
Colour	RAL 1000 green-beige (no modifications after 6 months at 4–8°C)
Physical State	Small granules
Odour	Odourless (no modifications after 6 months at 4–8°C)
Stability	stable after 6 months of storage at 4–8°C
Corrosion Characteristics	no evidence of corrosion was observed
pH	Initial: pH 1% aqueous suspension: 6.94 at 20.1°C After 6 months at 4–8°C: pH 1% aqueous suspension: 6.69 at 24.9°C
Density	0.448 g/mL pour density 0.496 g/mL tap density
Wettability	Initial: Static 2 sec, Dynamic 1 sec After 6 months at 4–8°C: Static 2 sec, Dynamic 1 sec
Persistence of Foaming	2 mL after 10 sec 2 mL after 1 min 1 mL after 3 min 0 mL after 12 min

Property	Result
Suspensibility	0.03% Suspension: Initial 100.06% After 6 months at 4–8ºC 100.78% 0.06% Suspension: Initial 99.12% After 6 months at 4–8ºC 100.17%
Spontaneity of Dispersion	Initial: 100.23% After 6 months at 4–8ºC: 102.21%
Wet Sieve Test	Initial: 0.01% After 6 months at 4–8ºC: 0.02%
Particle Size Distribution	Initial: X ≥ 1000µm =2.40% 1000 µm > x ≥ 850 µm =6.12% 850 µm > x ≥ 500 µm ≥= 28.86% 500 µm > x ≥ 355 µm ≥ =23.23% 355 µm > x ≥ 250 µm =18.56% 250 µm > x ≥ 125 µm =17.51% 125 µm > x ≥ 75 µm =2.71% After 6 months at 4–8°C: X ≥ 1000µm =2.51% 1000 µm > x ≥ 850 µm =4.09% 850 µm > x ≥ 500 µm ≥= 29.32% 500 µm > x ≥ 355 µm ≥ =24.25% 355 µm > x ≥ 250 µm =19.10% 250 µm > x ≥ 125 µm =17.21% 125 µm > x ≥ 75 µm =3.10%
Dust Content	Initial: 0.004% Nearly dust-free (1.2 mg) After 6 months at 4–8°C: 0.003%, Nearly dust-free (0.9 mg)
Friability and Attrition	Initial: Friability and attrition resistance 99.17% After 6 months at 4–8°C: Friability and attrition resistance 99.69%
Flowability	The sample flows naturally through the sieve.

1.3 Directions for Use

Trianum WG Biological Fungicide and Trianum G Biological Fungicide are soil-applied fungicides, applied in solution or mixed directly into the substrate, respectively, for the suppression of certain soil-borne root diseases. The guarantees for Trianum WG and Trianum G are a minimum of 1 x 10^9 colony forming units (CFU) and 1.5 x 10^8 CFU, respectively.

Trianum WG Biological Fungicide is applied at a rate of 1.5-3.0 g/m^2 or 15-30 g/1000 plants in greenhouse crops or greenhouse ornamentals, 1.5 g/m^2 or 3 kg/ha in field lettuce, 1.5-2.5 kg/ha in field carrots, and 15-30 g/100 m^2 in turf.

Trianum G Biological Fungicide is applied at a rate of 375-750 g/m^3 or 1 g/planting hole in greenhouse crops or greenhouse ornamentals, 15-25 kg/ha in field lettuce and field carrots, and 15-30 g/100 m^2 in turf.

1.4 Mode of Action

Trichoderma harzianum strain T-22 is a beneficial fungus that out-competes plant pathogenic fungi for space and nutrients, colonizing the plant roots ahead of the pathogens. It also acts as a mycoparasite by producing enzymes which break down the hyphae of the plant pathogenic fungi. The mechanisms of biocontrol with *T. harzianum* are complex, and generally considered with competition with plant pathogens for space and substrates in the rhizosphere, mycoparasitism and the secretion of cell wall degrading enzymes, production of antifungal substances, and induction of systemic resistance.

2.0 Methods of Analysis

2.1 Methods for Identification of the Microorganisms

T. harzianum strain T-22 can be identified to the species level using a combination of colony morphologies on agar media and cellular morphology. *T. harzianum* strain T-22 can also be identified to the strain level by sequencing the translation-elongation factor 1-α (*tef1*) and the rDNA (ribosomal deoxyribonucleic acid) internal transcribed spacer (ITS) genes as well as a combination of isozyme electrophoresis, colony morphology on differential medium, and universally primed polymerase chain reaction (UP-PCR) analysis.

2.2 Methods for Establishment of Purity of Seed Stock

The production strain is maintained as a master seed stock that is stored at -150°C. All stocks are tested for microbial contamination and integrity of the microbial pest control agent (MPCA). Practices for ensuring the purity and the integrity of the master seed stock were adequately described in the method of manufacture and quality assurance program.

2.3 Methods to Define the Content of the Microorganism in the Manufactured Material Used for the Production of Formulated Products

The guarantee of the technical grade active ingredient is expressed as the number of spores per gram. Representative data on a single batch of Trianum Technical was submitted.

The guarantee of the end-use products is expressed as the number of colony forming units (CFU) per gram. Representative data on five batches of each end-use product (in other words, Trianum G Biological Fungicide and Trianum WG Biological Fungicide) were submitted.

Representative data included spore counts, CFU counts, and/or gene sequencing results (ITS and *tef*).

2.4 Methods to Determine and Quantify Residues (Viable or Non-viable) of the Active Microorganism and Relevant Metabolites

As noted in Section 2.1, the MPCA can be identified to the strain level using a combination of gene sequences (ITS and *tef1*), isozyme electrophoresis and colony morphologies on differential medium. No methods are required to quantify viable or non-viable residues of *T. harzianum* strain T-22. *T. harzianum* is a ubiquitous microorganism in nature and has been isolated from a wide variety of environments. The use of strain T-22 is not expected to significantly increase the natural environmental background levels of this microorganism. Furthermore, when *T. harzianum* strain T-22 was administered orally to rats, no signs of toxicity or disease were observed.

Although secondary metabolites of toxicological significance (peptaibols) have been shown to be produced by naturally occurring strains of *T. harzianum* (including strain T-22), the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide is not expected to result in a sustained increase in levels of these peptaibols beyond the naturally occurring background levels from *T. harzianum* native strains. Due to the proteinaceous nature of these polypeptides, they are expected to be short lived in the environment once produced. They are susceptible to denaturing by ultraviolet light, high temperatures and various microbial processes in the environment. Furthermore, the results of supporting mammalian toxicity and pathogenicity studies did not indicate the presence of any metabolites of toxicological concern. No methodologies are required to quantify peptaibol residues.

2.5 Methods for Determination of Relevant Impurities in the Manufactured Material

The quality assurance procedures that will be used to limit contaminating microorganisms during manufacture of Trianum Technical, Trianum G Biological Fungicide and Trianum WG Biological Fungicide are acceptable.

During manufacturing, several approaches are used to limit microbial contamination in the technical grade active ingredient and end-use product. These approaches will include microscopic evaluations (cellular morphology), plating on selective agar media, sterilization of all equipment and media, and sanitization of recovery equipment.

The absence of human pathogens and below-threshold levels of contaminating microorganisms were shown in the microbial screening of production batches using microbe-specific screening methods for detecting and enumerating microbial contaminants of concern. Release standards for microbial contaminants comply with those permitted by the PMRA and are adequate to ensure that the end-use product does not contain unacceptable levels of human and animal disease-causing microorganisms.

2.6 Methods to Determine Storage Stability, Shelf-life of the Microorganism

Based on the results of a two-month storage stability study, the technical grade active ingredient is stable when stored at −18ºC for a period of up two months. Similarly, the end-use products were stable when stored at 4–12 ºC for a period of six months based on the results of six-month storage stability studies.

3.0 Impact on Human and Animal Health

3.1 Toxicity and Infectivity Summary

3.1.1 Test Studies

The PMRA conducted a detailed review of the toxicological studies submitted in support of the technical grade active ingredient, Trianum Technical, and the end-use products, Trianum G Biological Fungicide and Trianum WG Biological Fungicide.

The studies submitted to fulfil the requirements for health hazard assessment of the technical grade active ingredient, Trianum Technical, included acute oral toxicity/pathogenicity, acute pulmonary toxicity/pathogenicity, acute intravenous infectivity, dermal irritation, and eye irritation studies. The toxicity/pathogenicity studies were conducted with *T. harzianum* KRL-AG2 Powder or *T. harzianum* KRL-AG2 Paste. This test material was acceptable since strain KRL-AG2 is a synonym for strain T-22.

In the acute oral infectivity and toxicity study, groups of fasted, 6-week old rats (13/sex) were given a single oral dose of *T. harzianum* strain T-22 (nominal: 3.1×10^8 CFU/g) in sterile water at a dose of approximately 10^8 CFU/animal. The animals were then observed for a period of up to 21 days with interim sacrifices on Days 1, 7, 14, and 21 to evaluate clearance. There were no unscheduled mortalities observed throughout the study period and no treatment-related lesions noted in any of the animals. One female rat in the treatment group demonstrated lethargy, hunched posture and cessation of fecal and urine production beginning on Day 4. This animal appeared normal by Day 7. One male rat in the untreated group had a sore on the neck on Day 17. Also, one treated female rat lost weight by Day 7, but gained weight by study termination. At sacrifice, the MPCA was not detected in brain, lymph nodes, blood, kidney, spleen, liver, and lungs of any animal. The MPCA was detected in the feces of all treated rats on Day 1 but was cleared by Day 2. In this study, *T. harzianum* strain T-22 is of low toxicity and is not infective or pathogenic to the rat via the oral route.

In the acute pulmonary infectivity and toxicity study, groups of 45-day old Sprague Dawley rats (15/sex) were exposed by the intratracheal route to *T. harzianum* strain T-22 (nominal: 2.3×10^{10} CFU/g; measured: 2.7×10^{10} CFU/g) in saline at a dose of approximately 10^8 CFU/animal. Animals were then observed for up to 21 days with interim sacrifices on Days 1, 7, 14, and 21 to evaluate clearance. There were no unscheduled mortalities observed throughout the study period. All treated animals (male and female) appeared lethargic on the day of dosing. These animals recovered within one day after dosing and remained normal for the remainder of the study period. One treated female and two treated males lost weight between Days 14 and 21. At sacrifice, the MPCA was primarily detected in the lungs of treated male and female rats as well as in the brain, liver, blood, kidneys and spleens of treated rats. All counts were cleared or dramatically reduced by Day 21. At necropsy, mottled lungs were observed in 11/15 treated males and females, and enlargement of the lungs were observed in 6/15 treated males and females. These necropsy findings were considered normal immunological reactions to foreign material following the intratracheal instillation of a large concentration of foreign material. There were no unusual findings or observations in any of the untreated animals. In this study, *T. harzianum* strain T-22 is of low toxicity and is not infective or pathogenic to the rat via the pulmonary route.

In the acute intravenous infectivity study, groups of 44-day old Sprague Dawley rats (15/sex) were injected with *T. harzianum* strain T-22 (nominal: 2.3×10^{10} CFU/g; measured: 2.7×10^{10} CFU/g) in sterile normal saline at a dose of approximately 10^7 CFU/animal. Animals were then observed for up to 21 days with interim sacrifices on Days 1, 7, 14, and 21 to evaluate clearance. There were no unscheduled mortalities or any signs of clinical toxicity noted throughout the study period. One untreated female rat and one untreated male rat lost weight between Days 7 and 14, but gained weight by study termination. At sacrifice, MPCA was detected in various tissues of treated animals but primarily in the kidney, spleen, liver and lungs within 24 hours of injection. By Day 21, the MPCA had cleared from most tissues and the number of colonies was greatly reduced in the lungs and spleen. The MPCA was not observed in any of the untreated rats. At necropsy, treatment-related lesions were limited to an enlargement of the spleen in 9/15 treated rats of both sexes. No splenomegaly was observed in any untreated test animal. This necropsy finding was considered a normal immunological reaction to foreign material. In this study, *T. harzianum* strain T-22 was not pathogenic to the rat via the intravenous route.

In the dermal irritation study, ~15-week old New Zealand white rabbits (2♂, 1♀) were dermally exposed to 0.5 mL Trianum Technical ($>3\times10^9$ spores/g; $>2\times10^9$ CFU/g) for 4 hours to an area 2.5×2.5 cm. Animals then were observed for 72 hours. Irritation was scored by the method of Draize. No dermal irritation was noted during the entire study period. In this study, Trianum Technical was not irritating to the skin of rabbits (Maximum Irritation Score [MIS] 0/8; Maximum Average Score [MAS] 0/8 at 24, 48 and 72 h) and is uncategorized under the Globally Harmonized System of Classification and Labelling of Chemicals.

In the eye irritation study, 0.1 mL of Trianum Technical ($>3\times10^9$ spores/g; $>2\times10^9$ CFU/g) was instilled into the conjunctival sac of the right eye of young adult, New Zealand white rabbits (2♂, 1♀). All treated eyes were washed with room temperature deionized water for one minute immediately after recording the 24-hour observation. Animals were observed for 72 hours.

Irritation was scored by the method of Draize after 1, 24, 48 and 72 hours. There was no ocular irritation noted throughout the study period. In this study, Trianum Technical was not irritating to eyes of rabbits based on MAS and MIS scores of 0/110, and is uncategorized under the Globally Harmonized System of Classification and Labelling of Chemicals.

The studies submitted to fulfil the requirements for health hazard assessment of the end-use products, Trianum G Biological Fungicide and Trianum WG Biological Fungicide, include dermal irritation and eye irritation studies.

In a primary dermal irritation study, ~14–17-week old New Zealand white rabbits (2♂, 1♀) were dermally exposed to 500 mg Trianum WG Biological Fungicide (1.2×10^9 CFU/g) for 4 hours to an area 2.5×2.5 cm. Animals then were observed for 72 hours. Irritation was scored by the method of Draize. No dermal irritation was noted during the entire study period. In this study, Trianum WG Biological Fungicide was not irritating to the skin of rabbits (MIS 0/8; MAS 0/8 at 24, 48 and 72 h) and is uncategorized under the Globally Harmonized System of Classification and Labelling of Chemicals.

In another dermal irritation study, ~13–16-week old New Zealand white rabbits (1♂, 2♀) were dermally exposed to 500 mg Trianum G Biological Fungicide (2×10^8 CFU/g) for 4 hours to an area 2.5×2.5 cm. Animals then were observed for 72 hours. Irritation was scored by the method of Draize. No dermal irritation was noted during the entire study period. In this study, Trianum G Biological Fungicide was not irritating to the skin of rabbits (MIS 0/8; MAS 0/8 at 24, 48 and 72 h) and is uncategorized under the Globally Harmonized System of Classification and Labelling of Chemicals.

In an eye irritation study, 100 mg of Trianum WG Biological Fungicide (1.2×10^9 CFU/g) was instilled into the conjunctival sac of the right eye of young adult (13 weeks old), New Zealand white rabbits (1♂, 2♀). All treated eyes were washed with room temperature deionized water for one minute immediately after recording the 24-hour observation. Animals were observed for 72 hours. Irritation was scored by the method of Draize after 1, 24, 48 and 72 hours. Grade 1 conjunctival redness was observed in all treated eyes after 1 hour. All irritation cleared by 24 hours after patch removal. In this study, Trianum WG Biological Fungicide was considered minimally/slightly irritating to eyes of rabbits based on a MIS of 2/110 (1 h), and is uncategorized under the Globally Harmonized System of Classification and Labelling of Chemicals.

In another eye irritation study, 100 mg of Trianum G Biological Fungicide (2×10^8 CFU/g) was instilled into the conjunctival sac of the right eye of young adult (13–16 weeks old), New Zealand white rabbits (2♂, 1♀). All treated eyes were washed with room temperature deionized water for one minute immediately after recording the 24-hour observation. Animals were observed for 72 hours. Irritation was scored by the method of Draize after 1, 24, 48 and 72 hours. Grades 1–2 conjunctival redness was observed in 2/3 treated eyes after 1–48 hours. Grade 1 conjunctival chemosis and discharge were observed in one treated eye by 24 hours after patch removal. Slight dulling of the cornea and fluorescent staining were observed in one treated eye after 24 hours. No corneal effects were noted after 48 hours. All other irritation cleared by 72 hours after patch removal. In this study, Trianum G Biological Fungicide was considered

minimally/slightly irritating to eyes of rabbits based on a MIS of 3.33/110 (1 h), and is uncategorized under the Globally Harmonized System of Classification and Labelling of Chemicals.

These studies are summarized in Appendix I, Table 1.

3.1.2 Additional Information

Koppert Canada Limited submitted scientific rationales to waive acute dermal toxicity testing of Trianum G Biological Fungicide and Trianum WG Biological Fungicide. The rationales were based on the identity of the formulation ingredients, the absence of adverse effects (including hypersensitivity effects) reported for workers involved in the manufacture of the product, and the lack of overt effects noted in acute mammalian testing with Trianum Technical, Trianum G Biological Fungicide and Trianum WG Biological Fungicide. The requests to waive acute dermal toxicity testing were accepted.

Trichoderma spp. are able to produce different metabolites belonging to polyketides, sesquiterpenes (including the mycotoxin group of trichothecenes), viridofungins, and peptaibols. Some of these are inhibitory to fungi or bacteria; others have proven toxicity to mammals. There are no toxic effects known for strain T-22 and its metabolites. As noted in Section 2.4, strain T-22 can produce peptaibols, namely harzianins HBI and HC XII, and trichorzins HAII and HAV, under certain growing conditions. Despite the finding that *T. harzianum* strain T-22 produces peptaibols with documented biological activities, however, it is unlikely that the proposed use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide would significantly increase the background levels of these compounds due to the presence of naturally occurring *T. harzianum*. The accumulation of potentially toxic metabolites (including peptaibols) in the environment has not been observed to date and effects of antibiosis against bacteria or fungi were only demonstrated in vitro.

3.1.3 Incident Reports Related to Human and Animal Health

Since 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the Pesticides and Pest Management portion of Health Canada's website. Incidents were reviewed for the active ingredients, *T. harzianum* strains T-22 and KRL-AG2. As of 10 March 2014, no incident reports involving these strains of *T. harzianum* have been reported to the PMRA, the United States Environmental Protection Agency or the California Pesticide Illness Query database.

3.1.4 Hazard Analysis

The database submitted by Koppert Canada Limited in support of registering Trianum Technical, Trianum G Biological Fungicide and Trianum WG Biological Fungicide was reviewed from the viewpoint of human health and safety and was determined to be sufficiently complete to permit a decision on registration.

T. harzianum strain T-22 was of low toxicity and not infective or pathogenic to rats via the oral, pulmonary, and intravenous routes. In addition, Trianum Technical was not irritating to the skin or eyes of rabbits.

The end use products, Trianum G Biological Fungicide and Trianum WG Biological Fungicide, were not irritating to skin of rabbits and slightly/minimally irritating to the eyes of rabbits. Additionally, scientific rationales to waive acute dermal toxicity testing were deemed acceptable.

Although no reports of hypersensitivity incidents among workers were reported by the applicant, Koppert Canada Limited, the signal words "POTENTIAL SENSITIZER" will appear on the labels for the technical grade active ingredient and end-use products as all microorganisms are recognized as being able to produce substances that can elicit allergic reactions after repeated exposure to high concentrations.

Higher tier subchronic and chronic toxicity studies were not required because of the low acute toxicity of the end-use products, and no indications of infectivity, toxicity or pathogenicity of *T. harzianum* strain T-22 in the test animals treated in the Tier I acute oral, pulmonary, intravenous, toxicity/infectivity tests.

Within the available scientific literature, there are no reports that suggest *T. harzianum* strain T-22 has the potential to cause adverse effects on the endocrine system of animals. Based on the weight of evidence of available data, no adverse effects to the endocrine or immune systems are anticipated for *T. harzianum* strain T-22.

3.2 Occupational, Residential and Bystander Risk Assessment

3.2.1 Occupational Exposure and Risk

When handled according to the label instructions, the potential for dermal, eye and inhalation exposure for applicators, mixer/loaders, and handlers exists, with primary exposure route being dermal. Since unbroken skin is a natural barrier to microbial invasion of the human body, dermal absorption could occur only if the skin were cut, if the microbe were a pathogen equipped with mechanisms for entry through or infection of the skin, or if metabolites were produced that could be dermally absorbed. *T. harzianum* strain T-22 has not been identified as a dermal wound pathogen and does not contain any known toxic secondary metabolites. There is no indication that it could penetrate intact skin of healthy individuals. Furthermore, toxicity testing with *T. harzianum* strain T-22, Trianum G Biological Fungicide and Trianum WG Biological Fungicide showed no significant signs of toxicity via the oral or pulmonary routes of exposure, and no dermal toxicity to Trianum G Biological Fungicide and Trianum WG Biological Fungicide is anticipated. The submitted eye and dermal irritation studies with Trianum G Biological Fungicide and Trianum WG Biological Fungicide demonstrated minimal eye and skin irritation.

Although toxicity from dermal or inhalation exposure is considered minimal from the proposed end-use product use, the PMRA assumes that all microorganisms contain substances that can elicit positive hypersensitivity reactions, regardless of the outcome of sensitization testing. Therefore, anyone handling or applying Trianum G Biological Fungicide and Trianum WG Biological Fungicide must wear waterproof gloves, long-sleeved shirts, long pants, a dust/mist filtering respirator/mask (NIOSH approval number prefix TC-21) or NIOSH approved respirators (with any N-95, P-95, R-95 or HE filter), and shoes plus socks. In addition, all unprotected workers are restricted from entering enclosed areas (including greenhouses) where Trianum WG Biological Fungicide and Trianum G Biological Fungicide have been handled or applied to soil until dusts have settled.

Label warnings, restrictions and risk mitigation measures are adequate to protect users of Trianum G Biological Fungicide and Trianum WG Biological Fungicide, and no significant occupational risks are anticipated for these products.

3.2.2 Residential and Bystander Exposure and Risk

Adults, youths and toddlers may be exposed to *T. harzianum* strain T-22 by the use of Trianum WG Biological Fungicide and Trianum G Biological Fungicide on agricultural crops, ornamentals and turf. Overall, the PMRA does not expect that residential and bystander exposures will pose an undue risk on the basis of the low toxicity/pathogenicity profile for *T. harzianum* strain T-22, Trianum Technical, Trianum G Biological Fungicide and Trianum WG Biological Fungicide, and the assumption that precautionary label statements will be followed by commercial applicators in the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide. As well, *T. harzianum* is a species that is ubiquitous in the environment and the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide is not expected to cause sustained increases in exposure to bystanders beyond natural levels. Consequently, the health risk to infants and children is expected to be negligible.

3.3 Dietary Exposure and Risk Assessment

3.3.1 Food

Although the proposed use pattern may result in some dietary exposure with possible residues in or on agricultural commodities, negligible to no risk is expected for the general population, including infants and children, or animals because *T. harzianum* strain T-22 demonstrated no pathogenicity, infectivity or oral toxicity at the maximum dose tested in the Tier I acute oral toxicity/infectivity study. Furthermore, higher tier subchronic and chronic dietary exposure studies were not required because of the low toxicity of the MPCA and no indications of infectivity, toxicity or pathogenicity in the test animals treated in the Tier I acute oral and pulmonary toxicity/infectivity studies. Although dietary exposure to peptaibols produced by strain T-22 may be possible from consumption of foliage or fruits of food commodities treated with *T. harzianum* strain T-22, the level of these peptaibols remaining on leaf or fruit surfaces is expected to be low as the peptaibols are proteinaceous in nature and easily denatured by ultraviolet light, low humidity and other microbial processes present in the environment. In addition, these residues may be removed by washing, peeling or processing of commodities. Uptake of fungal metabolites by plants and translocation to fruit is possible for metabolites produced by the actively growing fungus in soil treated with Trianum G Biological Fungicide and Trianum WG Biological Fungicide, but no crop residue data were submitted for any of the secondary metabolites that may present a human health concern, specifically peptaibol antibiotics. However, analytical data on the peptaibol production levels from strain T-22 relative to at least one other naturally occurring strain of *T. harzianum* suggest the MPCA produces peptaibols at levels unlikely to exceed those produced by naturally occurring isolates in the environment. Consequently, the risk from secondary metabolites to the general population, including infants and children, or animals are negligible. Furthermore, there are no concerns for chronic risks posed by dietary exposure of the general population and sensitive subpopulations, such as infants and children.

3.3.2 Drinking Water

No risks are expected from exposure to this microorganism via drinking water because exposure will be minimal and because there were no harmful effects observed in Tier I acute oral toxicity testing and infectivity testing. The end use product labels instruct users not to contaminate irrigation or drinking water supplies or aquatic habitats through equipment cleaning or waste disposal. Users are also requested not to allow effluent or runoff from greenhouses containing this product to enter lakes, streams, ponds or other waters. Furthermore, municipal treatment of drinking water is expected to remove the transfer of residues to drinking water. Therefore, potential exposure to *T. harzianum* strain T-22 in surface and drinking water is negligible.

3.3.3 Acute and Chronic Dietary Risks for Sensitive Subpopulations

Calculations of acute reference doses (ARDs) and acceptable daily intakes (ADIs) are not usually possible for predicting acute and long term effects of microbial agents in the general population or to potentially sensitive subpopulations, particularly infants and children. The single

(maximum hazard) dose approach to testing MPCAs is sufficient for conducting a reasonable general assessment of risk if no significant adverse effects (in other words, no acute toxicity, infectivity or pathogenicity endpoints of concern) are noted in acute toxicity and infectivity tests. Based on all the available information and hazard data, the PMRA concludes that the *T. harzianum* strain T-22 is of low toxicity, is not pathogenic or infective to mammals, and that infants and children are likely to be no more sensitive to the MPCA than the general population. Thus there are no threshold effects of concern and, as a result, no need to require definitive (multiple dose) testing or apply uncertainty factors to account for intra- and interspecies variability, safety factors or margins of exposure. Further factoring of consumption patterns among infants and children, special susceptibility in these subpopulations to the effects of the MPCA, including neurological effects from pre- or post-natal exposures, and cumulative effects on infants and children of the MPCA and other registered micro-organisms that have a common mechanism of toxicity, does not apply to this MPCA. As a result, the PMRA has not used a margin of exposure (safety) approach to assess the risks of *T. harzianum* strain T-22 to human health.

3.3.4 Aggregate Exposure and Risk

Based on the toxicity and infectivity test data submitted and other relevant information in the PMRA's files, there is reasonable certainty that no harm will result from aggregate exposure of residues of *T. harzianum* strain T-22 to the general Canadian population, including infants and children, when the end-use product is used as labelled. This includes all anticipated dietary (food and drinking water) exposures and all other non-occupational exposures (dermal and inhalation) for which there is reliable information. Furthermore, few adverse effects from exposure to other isolates of *T. harzianum* encountered in the environment have been reported. Even if there is an increase in exposure to this active ingredient from the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide, there should not be any increase in potential human health risk.

3.3.5 Maximum Residue Limits

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine whether the consumption of the maximum amount of residues, that are expected to remain on food products when a pesticide is used according to label directions, will not be a concern to human health. This maximum amount of residues expected is then legally established as a maximum residue limit (MRL) under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act*. Health Canada sets science-based MRLs to ensure the food Canadians eat is safe.

T. harzianum are ubiquitous organisms found in most terrestrial environments. Residues of *T. harzianum* strain T-22 and its metabolites on treated food crops, at the time of harvest, are only anticipated following foliar applications to agricultural crops. Dietary exposure, however, is likely to be low since the MPCA is comprised of environmentally-sensitive short-lived spores that are not persistent on the phyllosphere. The PMRA has applied a hazard-based approach for determining whether an MRL is required for this microorganism. Although *T. harzianum* strain T-22 is known to produce secondary metabolites of toxicological significance, the secondary

metabolites are expected to have a short residency time in the environment. As such, the level of anticipated exposure to any potential secondary metabolites produced by the MPCA or residues of the MPCA itself is extremely low. No adverse effects from dietary exposure have been attributed to natural populations of *T. harzianum*, and no adverse effects were observed in the acute oral toxicity and infectivity study with *T. harzianum* strain T-22. Furthermore, there have been no reports of adverse effects to humans from natural populations of *T. harzianum*. In addition, the likelihood of residues contaminating drinking water supplies is negligible to non-existent. Therefore, the PMRA has determined that an MRL does not need to be established for *T. harzianum* strain T-22.

3.4 Cumulative Effects

The PMRA has considered available information on the cumulative effects of residues and other substances that have a common mechanism of toxicity. These considerations included the cumulative effects on infants and children of such residues and other substances with a common mechanism of toxicity. Besides naturally occurring strains of *T. harzianum* in the environment, the PMRA is not aware of any other microorganisms, or other substances that share a common mechanism of toxicity with *T. harzianum* strain T-22 (other than its synonym, strain KRL-AG2). No cumulative effects are anticipated if the residues of *T. harzianum* strain T-22 interact with related strains of this microbial species.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Trichoderma species are ubiquitous soil-dwellers, inhabiting soil, rotting wood and vegetable matter in virtually all terrestrial environments. They produce copious conidia held together in mucoid spore balls, which can be disseminated by water and by soil fauna such as insects and earthworms. With respect to its abundance relative to other species of *Trichoderma*, *T. harzianum* has been described as more characteristic of warm climates; however, it is evident that cold-tolerant strains do exist. It is also evident that *T. harzianum* KRL-AG2 will likely disseminate and persist in the Canadian environment following its release. The applicant submitted a field study report that evaluated the ability of strain T-22 to survive over the winter and to colonize subsequent crops. In this study, *T. harzianum* strain T-22 was detected in soil collected from the plots in the spring of 1989 and thus survived over the winter. Its isolation from soils collected from untreated crops suggested that the active ingredient was rapidly disseminated in soil. Surviving populations of *T. harzianum* strain T-22 were shown to colonize roots of subsequent crops.

T. harzianum strain T-22 is not expected to persist in the phyllosphere. Ordinary environmental conditions cause rapidly declining population levels of this species soon after application to above-ground plant parts.

Although there may be some potential for surface water exposure resulting from spray drift from field applications or run-off events, the concentration of *T. harzianum* strain T-22, which are deposited in surface water bodies, are expected to be at or below naturally occurring background levels. Few reports, however, have cited instances of recovery of *Trichoderma* spp. from fresh or salt water environments unless the water was polluted. The lack of evidence on the natural occurrence of *T. harzianum* in freshwater or salt water indicates a failure to establish itself in these environments.

The use of Trianum WG Biological Fungicide and Trianum G Biological Fungicide is not expected to result in a sustained increase in levels of *T. harzianum* strain T-22 and its associated metabolites (for example, peptaibols) beyond the naturally occurring background levels of those produced by native *T. harzianum* strains.

4.2 Effects on Non-Target Species

PMRA has a four-level tiered approach to environmental testing of microbial pesticides. Tier I studies consist of acute studies on up to seven broad taxonomic groups of non-target organisms exposed to a maximum hazard or Maximum Challenge Concentration (MCC) of the microbial pest control agent (MPCA). The MCC is generally derived from the amount of the MPCA or its toxin expected to be available following application at the maximum recommended label rate multiplied by some safety factor. Tier II studies consist of environmental fate (persistence and dispersal) studies as well as additional acute toxicity testing of MPCAs. Tier III studies consist of chronic toxicity studies (this is, life cycle studies) as well as definitive toxicity testing, for example, LC_{50}, LD_{50}. Tier IV studies consist of experimental field studies on toxicity and fate, and are required to determine whether adverse effects are realized under actual use conditions.

The type of environmental risk assessment conducted on MPCAs varies depending on the tier level that was triggered during testing. For many MPCAs, Tier I studies are sufficient to conduct environmental risk assessments. Tier I studies are designed to represent “worst-case” scenarios where the exposure conditions greatly exceed the expected environmental concentrations. The absence of adverse effects in Tier I studies are interpreted as minimal risk to the group of non-target organisms. However, higher tiered studies will be triggered if significant adverse effects on non-target organisms are identified in Tier I studies. These studies provide additional information that allows PMRA to refine the environmental risk assessments. In the absence of adequate environmental fate and/or field studies, a screening level risk assessment can be performed to determine if the MPCA is likely to pose a risk to a group of non-target organisms. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC).

If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (environmental fate and/or field testing results). Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Effects on Terrestrial Organisms

Two studies were submitted to address the hazards of the *T. harzianum* strain T-22 to terrestrial non-target organisms. These studies included non-target avian species and arthropods. The non-target bird study was conducted with *T. harzianum* strain KRL-AG2. This test material was acceptable since strain KRL-AG2 is a synonym for strain T-22.

The acute oral toxicity of *T. harzianum* strain T-22 to 21-day-old Bobwhite (*Colinus virginianus*) was assessed over 30 days. In this study, *T. harzianum* strain T-22 was administered to 42 birds by oral gavage at 2 222 mg a.i./kg bw (or approximately 9×10^8 CFU/kg bw) per day for five days which is equivalent to 11 110 mg/kg bw (or approximately 4×10^9 CFU/kg bw). There were no mortalities, signs of toxicity or apparent effects on body weight or feed consumption among the treated birds. One bird in the treated group was noted with enlarged adrenal glands, but this observation was not considered treatment-related as the adrenal glands in the other 41 treated birds appeared normal. There were no signs of toxicity and there were no mortalities. When compared to the negative, attenuated and sterile filtrate controls, there were no apparent effects on body weight or feed consumption among the treated birds. The 30-day acute oral LD_{50} was greater than 9×10^8 CFU/kg bw per day for five consecutive days.

In a published article, the lethal and sublethal effects of a selection of seven microbiological control agents, including Trianum-P (=Trianum WG Biological Fungicide), were investigated in bumblebees following contact and ingestion exposures. To determine the effect of strain T-22 on the survival and reproduction of bumblebees, adult worker bees were placed in artificial nest boxes and exposed at 1/1, 1/2, 1/5, and 1/10 maximum field recommended concentrations via contact by topical application, and orally via treated sugar water and via treated pollen. The maximum field recommended concentration for *T. harzianum* strain T-22 was 0.06 % w/v. For each treatment, worker mortality was scored after 72 h and on a weekly basis during a period of 11 weeks. To determine the sublethal effects of the strain T-22 on foraging behaviour of bumblebees, adult workers were placed in artificial nest boxes that connected to a second nesting box by a tube of approximately 20 cm length and 2 cm diameter. In one box (A), the workers constructed their nest. After 2 weeks, when third- and fourth-instar larvae appeared in the nests, food was removed from box A and placed in box B. Before exposure to strain T-22, the workers were allowed a training period of 2 days to forage for untreated food in box B. Afterwards, the sugar water in box B was replaced with sugar water treated with strain T-22 at its maximum field recommended concentrations. Worker survival and drone production were scored on a weekly basis, in a similar manner to that described above, over a period of 9 weeks. No lethal effects on the survival of worker bumblebees or sublethal effects on reproduction and foraging behaviour were observed for *T. harzianum* strain T-22.

No toxicity/pathogenicity data were considered to address the potential for harm to wild mammals, other beneficial arthropods, non-arthropod invertebrates, microorganisms and terrestrial plants. Scientific rationales were submitted to address these groups of non-target organisms as well as avian inhalation. The potential harm to wild mammals was also addressed with human health studies.

Trichoderma species are ubiquitous in virtually all terrestrial environments. *T. harzianum* occurs worldwide in all kinds of soils, including agriculture, forests and orchards. *T. harzianum* is particularly abundant in the rhizosphere, and occurs also on decaying plant material. No particular soil type is required by *T. harzianum*. It is a saprophytic fungus that degrades organic matter, mainly derived from plants. *T. harzianum* is often closely associated to plant roots and is able to parasitize other fungi, particularly plant pathogens. *T. harzianum* is not restricted to a particular host.

Trichoderma spp. are prolific producers of various proteins, enzymes and metabolites that are inhibitory to fungi or bacteria, demonstrate some toxicity to mammals, and others appear to induce growth regulation or systemic resistance in plants. For example, some isolates of *T. harzianum* produce harzianolide. In studies, harzianolide significantly increased tomato seedling growth by inducing the expression of genes involved in the salicylic acid (PR1 and GLU) and jasmonate/ethylene (JERF3) signaling pathways. Trichodiene is also reportedly involved in the induction of systemic resistance in plants. A study showed that strain T-22 can indeed produce harzianins HBI and HC XII, and trichorzins HAII and HAV when cultured under specific growing conditions. However, no toxic effects were observed in the avian oral study with Northern Bobwhite quail after *T. harzianum* strain T-22 was administered to birds nor were any toxic effects observed in bumblebees following contact and dietary exposures. Although it is possible for this strain to produce these toxic metabolites following application, the accumulation of potentially toxic metabolites in the environment due to naturally occurring isolates has not been observed to date despite the ubiquitous nature of this organism. These peptaibols and metabolites are likely degraded and/or detoxified quickly due to photolysis and/or enzymatic activity in soil.

Searches through PubMed using the various keywords have yielded no reports of adverse effects to birds, wild mammals, arthropods and non-arthropod invertebrates. A single report concluding that the culture filtrate of an isolate of *T. harzianum* reduced various parameters of root and shoot growth in wheat seedlings was found. The vast majority of published studies reported beneficial effects through biological control of plant pathogens and/or through the induction of systemic resistance in various plants following colonization of the plant rhizosphere. *T. harzianum* is not generally considered a pathogen of birds, mammals, arthropods, non-arthropod invertebrates or plants. Furthermore, strain T-22 does not seem to grow at temperatures of 37°C or above thus limiting its ability to colonize birds and mammals.

From the data submitted under Section 3.1.1, it was determined that *T. harzianum* strain T-22 was not toxic or pathogenic to mammals via the oral, pulmonary, and intravenous routes.

T. harzianum is a fungal pathogen and many isolates reportedly produce enzymes and metabolites which could adversely affect non-target microorganisms. Parasitism on cultivated mushrooms, "green mould disease", which was originally assigned to *T. harzianum,* is now known to occur only in the related species *T. aggressivum*. This species is morphologically similar, but can be clearly distinguished from biocontrol strains of *T. harzianum* using molecular methods. No additional microorganism testing is required even though the product is intended to control pest microorganisms, as *T. harzianum* is a normal component of the soil, and the organism is not expected to affect environmentally or economically important microbial species or microbiologically mediated biogeochemical processes.

Based on all the available data and information on the effects of *T. harzianum* strain T-22 to non-target terrestrial organisms, there is reasonable certainty that no harm will be caused to birds, wild mammals, arthropods (including honeybees), non-arthropod invertebrates, non-target microorganisms and plants from the proposed use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide.

4.2.2 Effects on Aquatic Organisms

No studies were submitted to address the hazards of the technical grade active ingredient to aquatic non-target organisms. Instead scientific rationales were submitted to waive the data requirements for all aquatic non-target testing. These rationales were based on minimal exposure due to the products' proposed use patterns, the ubiquitous nature of *T. harzianum*, lack of reported adverse effects in the literature and the inability of *T. harzianum* to become established in unpolluted aquatic environments.

Independent searches through PubMed using the various keywords have yielded no reports of adverse effects to fish, aquatic arthropods, aquatic non-arthropod invertebrates and aquatic plants.

Based on all the available data and information on the effects of *T. harzianum* strain T-22 to non-target aquatic organisms and the precautionary measures required on the labels of Trianum G Biological Fungicide and Trianum WG Biological Fungicide, there is reasonable certainty that no harm will be caused to fish, aquatic arthropods and non-arthropod invertebrates, and aquatic plants from their proposed uses.

4.3 Incident Reports related to the Environment

Since 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra. Only incidents in which the pesticide is determined to be linked to the effects (Canadian causality of highly probable, probable and possible; American causality of highly probable, probable and possible) are considered in the reviews.

As of 10 March 2014, there were no environmental incidents reported in the PMRA Incident reporting database or in the United States' Ecological Incident Information System (EIIS) for products containing *T. harzianum* strains T-22 and KRL-AG2 (synonym) for use as pesticides.

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Acceptable Efficacy Claims

5.1.1.1 Greenhouse lettuce

Post-emergence damping off (*Rhizoctonia solani*): Efficacy data from two trials, conducted in 2011 in the Netherlands, were provided where Trianum WG Biological Fungicide was applied at the proposed rate. Based on the timing of the assessment a claim of suppression of post-emergence damping off (*Rhizoctonia solani*) on greenhouse lettuce could be supported on the Trianum WG label. Efficacy data from four trials, conducted in 2011 in the Netherlands, were provided where Trianum G was applied at the proposed rate. Based on the timing of the assessment a claim of suppression of post-emergence damping off (*Rhizoctonia solani*) on greenhouse lettuce could be supported on the Trianum G Biological Fungicide label.

5.1.1.2 Field lettuce

Post-emergence damping off (*Rhizoctonia solani*): Based on the value information provided in support of the claim of post-emergence damping off (*Rhizoctonia solani*) on greenhouse lettuce, an extrapolation was possible for this claim on the Trianum WG Biological Fungicide and the Trianum G Biological Fungicide labels. The level of efficacy achieved on field lettuce is expected to be comparable to that of greenhouse lettuce.

5.1.1.3 Greenhouse Tomatoes

Fusarium root rot and Fusarium crown rot (*Fusarium oxysporum*): Efficacy data from five trials, conducted in the Netherlands, Spain and Romania from 2010-2011, were provided where Trianum WG Biological Fungicide was applied at the proposed rate. Based on the parameters assessed a claim of suppression of fusarium root rot and fusarium crown rot (*Fusarium oxysporum*) on greenhouse tomatoes could be supported on the Trianum WG Biological Fungicide label. Efficacy data from four trials, conducted in the Netherlands, Spain and Romania from 2010-2012, were provided where Trianum G Biological Fungicide was applied at the proposed rate. Based on the parameters assessed a claim of suppression of fusarium root rot and fusarium crown rot (*Fusarium oxysporum*) on greenhouse tomatoes could be supported on the Trianum G Biological Fungicide label.

5.1.1.3 Greenhouse Cucumbers

Post-emergence damping off (*Pythium ultimum*): Efficacy data from three trials, conducted in the Netherlands and Spain in 2011, were provided where Trianum WG Biological Fungicide was applied at the proposed rate. Based on the parameters assessed a claim of suppression of post-emergence damping off (*Pythium ultimum*) on greenhouse cucumbers could be supported on the Trianum WG Biological Fungicide label. Efficacy data from two trials, both conducted in the Netherlands in 2011, were provided where Trianum G Biological Fungicide was applied at the proposed rate. Based on the parameters assessed a claim of suppression of post-emergence damping off (*Pythium ultimum*) on greenhouse cucumbers could be supported on the Trianum G Biological Fungicide label.

Pythium root rot (*Pythium aphanidermatum*): This claim is proposed for the Trianum G Biological Fungicide label only. Efficacy data from a single trial, conducted in Spain in 20011, were provided where Trianum G Biological Fungicide was applied at the proposed rate. Based on the results from this trial, and given that the claim of suppression for *P. ultimum* is supported on greenhouse cucumbers and a claim for *P. violae* is supported on carrots, a claim of suppression of pythium root rot (*P. aphanidermatum*) on greenhouse cucumbers could be supported on the Trianum G Biological Fungicide label.

5.1.1.4 Field Carrots

Cavity spot (*Pythium violae*): Efficacy data from two trials, conducted in the Netherlands and the United Kingdom from 2011-2012, were provided where Trianum WG Biological Fungicide was applied at the proposed rate. Based on the results a claim of suppression of cavity spot (*Pythium violae*) on field carrots could be supported on the Trianum WG Biological Fungicide label. Efficacy data from four trials, conducted in the Netherlands and the UK from 2011-2013, were provided where Trianum G Biological Fungicide was applied at the proposed rate. Based on the results a claim of suppression of cavity spot (*Pythium violae*) on field carrots could be supported on the Trianum G Biological Fungicide label.

Pythium root rot (*Pythium ultimum*) and post-emergence damping off (*Pythium ultimum*): These claims are proposed for the Trianum G Biological Fungicide label only. Based on the value information provided in support of the claim of post-emergence damping off (*P. ultimum*) on greenhouse cucumbers and claim of suppression of pythium root rot (*P. ultimum*) on saintpaulia, an extrapolation was possible for these claims on the Trianum G Biological Fungicide label. The level of efficacy achieved on field carrots is expected to be comparable to that of greenhouse cucumbers and greenhouse saintpaulia.

5.1.1.5 Greenhouse Carrots

Cavity spot (*Pythium violae*): This claim is proposed for the Trianum G Biological Fungicide label only. Based on the value information provided in support of the claim of cavity spot (*P. violae*) on field carrots, an extrapolation was possible for this claim on the Trianum G Biological Fungicide label. The level of efficacy achieved on field carrots is expected to be comparable to that of greenhouse carrots.

Pythium root rot (*Pythium ultimum*) and post-emergence damping off (*Pythium ultimum*): These claims are proposed for the Trianum G Biological Fungicide label only. Based on the value information provided in support of the claim of post-emergence damping off (*P. ultimum*) on greenhouse cucumbers and claim of suppression of pythium root rot (*P. ultimum*) on saintpaulia, an extrapolation was possible for these claims on the Trianum G Biological Fungicide label. The level of efficacy achieved on greenhouse carrots is expected to be comparable to that of greenhouse cucumbers and greenhouse saintpaulia.

5.1.1.6 Greenhouse Ornamentals

Post-emergence damping off (*Pythium ultimum*): This claim is proposed for both the Trianum WG Biological Fungicide and the Trianum G Biological Fungicide labels for the following ornamentals: saintpaulia, chrysanthemum and pansy. Efficacy data from four trials on saintpaulia (treatments with both formulations) and one trial on pansy (treatment with Trianum WG Biological Fungicide only), where the treatments were applied at the proposed rates, were provided. These five trials were conducted in the Netherlands and France in 2004 and 2012. Data on growth parameters were reported for the four trials on saintpaulia. Disease incidence was reported for the trial conducted on pansy. Growth parameters alone are insufficient to determine the level of efficacy expected from a proposed use. However, given that a claim of suppression of post-emergence damping off (*P. ultimum*) was supported for greenhouse cucumbers and that a claim of suppression of root diseases caused by Pythium on greenhouse ornamentals appears on the product labels containing *T. harzianum*, a claim of suppression of post-emergence damping off (*P. ultimum*) on saintpaulia, chrysanthemum and pansy, on both the Trianum WG Biological Fungicide and the Trianum G Biological Fungicide labels, could be supported.

Fusarium root rot and Fusarium crown rot (*Fusarium oxysporum*): These claims are proposed for both the Trianum WG Biological Fungicide and the Trianum G Biological Fungicide labels for the following ornamentals: saintpaulia, chrysanthemum and pansy. Efficacy data from four trials on chrysanthemum (three trials with both formulations; one trial with Trianum G Biological Fungicide only) where the treatments were applied at the proposed rates, were provided. These trials were conducted in the Netherlands in 2012. In all four trials, the pest pressure was too low to draw any conclusions. However, given that a claim of suppression of fusarium root rot and fusarium crown rot (*F. oxysporum*) was supported on greenhouse tomatoes, for both labels, a similar claim could also be supported on greenhouse ornamentals.

Extrapolation to all ornamentals: Although the applicant had only originally proposed the use of Trianum WG Biological Fungicide and Trianum G Biological Fungicide on three specific ornamentals, from a value perspective the use of these products could be supported on all ornamentals, for supported claims, provided that a standard statement, regarding pre-testing on a limited scale prior to large scale applications, was included on the label. The applicant indicated that they wished to include ornamentals, in general, on both labels.

5.1.1.7 Turf

Dollar spot (*Sclerotinia homoeocarpa*): Efficacy data from six trials, conducted in the UK and France from 2010-2011, were provided where both Trianum WG Biological Fungicide and Trianum G Biological Fungicide treatments were applied at the proposed rate. Based on the level of efficacy observed a claim of "reduces symptoms of dollar spot (*Sclerotinia homoeocarpa*)", rather than suppression, could be supported for both labels.

Microdochium patch (*Microdochium nivale*): Efficacy data from a single trial, conducted in the UK from 2010, were provided where both Trianum WG Biological Fungicide and Trianum G Biological Fungicide treatments were applied at the proposed rate. Based on the level of efficacy observed a claim of "reduces symptoms of Microdochium patch (*Microdochium nivale*)", rather than suppression could be supported for both labels.

5.1.1.8 Application Methods

Drench and pre-plant spray were supported as application methods. No information was provided in support of the drip-irrigation method.

5.2 Non-Safety Adverse Effects

No phytotoxicity was reported in host plants in any of the trials for which efficacy data were provided.

5.3 Consideration of Benefits

5.3.1 Social and Economic Impact

Of all the proposed uses, only one is listed as a priority in the Canadian Grower Priority Database (GPD): *T. harzianum* for the management of cavity spot on carrots. It is listed as a low priority. This claim, suppression of cavity spot on both field and greenhouse carrots, is supported for both Trianum WG Biological Fungicide and Trianum G Biological Fungicide. Control of damping off on field lettuce is listed as an intermediate priority in the GPD. Post-emergence damping off (*Pythium ultimum*) on field lettuce was supported. Although Trianum WG Biological Fungicide and Trianum G Biological Fungicide have not been identified as priorities solutions for post-emergence damping off on field lettuce, these products have value as they provide another solution in the management of this problem.

5.3.2 Survey of Alternatives

Alternatives exist for most of the proposed uses, consisting mainly of biological products for the greenhouse crops and field lettuce and mainly conventional products for turf and field carrots. For the uses that do have alternatives, the number of alternatives for each disease/crop combination ranges from one to 11 (see Table 3 in Appendix 1). For the following disease/crop combinations, this registration will provide a solution for which no alternative exists: post-emergence damping off (*R. solani*) on greenhouse lettuce, fusarium crown rot (*F. oxysporum*) on

greenhouse tomato, fusarium crown rot (*F. oxysporum*) on greenhouse ornamentals, cavity spot (*P. violae*) on greenhouse carrots and field carrots, pythium root rot (*P. ultimum*) on greenhouse carrots and field carrots, post-emergence damping off (*P. ultimum*) on greenhouse carrots and field carrots.

5.3.3 Compatibility with Current Management Practices Including Integrated Pest Management

The active ingredient, *T. harzianum* strain T-22, is a naturally occurring soil microorganism and would therefore be considered part of a grower Integrated Pest Management strategy.

5.3.4 Information on the Occurrence or Possible Occurrence of the Development of Resistance

The risk for resistance development is low given that these are biological products.

5.3.5 Contribution to Risk Reduction

Trianum Biological Fungicides contribute to the suppression and management of plant diseases that might otherwise require frequent application of conventional fungicides for disease control. The use of Trianum Biological Fungicides may help reduce conventional fungicide use in greenhouses and the field.

5.3.6 Health, Safety, and Environmental Benefits

Not applicable.

5.4 Supported Uses

Based on the value information proved, for all proposed pathogen/crop combinations, at least one disease (symptom) was supported. However for some pathogen/crop combinations, not all diseases were supported due to lack of supporting value information. In addition two disease claims on turf, dollar spot and microdochium patch, were amended from suppression to "may reduce symptoms of". For these two turf diseases, although the proposed treatment did have an effect on the disease, the level of control was below what is considered acceptable for a suppression claim. Drench and pre-plant spray were supported as application methods. No information was provided in support of the proposed drip-irrigation method. The supported claims for Trianum WG greenhouse and Trianum G greenhouse are shown in Table 4 of Appendix 1.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy: in other words, persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*.

Trianum Technical, Trianum G Biological Fungicide and Trianum WG Biological Fungicide were assessed in accordance with the PMRA Regulatory Directive DIR99-03.[5]

- Trianum Technical does not meet the Track 1 criteria because the active ingredient is a biological organism and hence is not subject to the criteria used to define persistence, bioaccumulation and toxicity properties of chemical control products.
- There are also no formulants, contaminants or impurities present in the end-use product that would meet the TSMP Track-1 criteria.

6.2 Formulants and Contaminants of Health Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette.*[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including DIR99-03 and DIR2006-02[8] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

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5 Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

6 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-11-30) pages 2641-2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613: *Part I Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

7 Notice of Intent NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*

8 Regulatory Directive DIR2006-02, *PMRA Formulants Policy*

- The technical grade active ingredient, Trianum Technical, does not contain formulants of health or environmental concern as identified in the *Canada Gazette,* Part II, Volume 139, Number 24, pages 2641-2643: *List of Pest Control Product Formulants of Health or Environmental Concern*.

- The end-use products, Trianum G Biological Fungicide and Trianum WG Biological Fungicide, do not contain formulants of health or environmental concern as identified in the *Canada Gazette,* Part II, Volume 139, Number 24, pages 2641-2643: *List of Pest Control Product Formulants of Health or Environmental Concern*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and DIR2006–02.

7.0 Summary

7.1 Methods for Analysis of the Micro-organism as Manufactured

The product characterization data for Trianum Technical, Trianum G Biological Fungicide and Trianum WG Biological Fungicide were judged to be adequate to assess their potential human health and environmental risks. The technical grade active ingredient was characterized and the specifications of the end-use product were supported by the analyses of a sufficient number of batches. Storage stability data were sufficient to support a shelf life of up to six months for the end-use product when stored at temperatures 4–12°C and up to two months for the technical grade active ingredient at −18°C.

7.2 Human Health and Safety

The acute toxicity and infectivity studies and other relevant information submitted in support of *T. harzianum* strain T-22 were determined to be sufficiently complete to permit a decision on registration. Submitted information suggests *T. harzianum* strain T-22 to be of low toxicity and not infective or pathogentic by the oral, pulmonary and intravenous routes. The information also suggests that Trianum Technical is not irritating to the skin and eyes. Similarly, Trianum G Biological Fungicide and Trianum WG Biological Fungicide are not irritating to the skin and slightly minimally irritating to the eyes. Since Trianum Technical, Trianum G Biological Fungicide and Trianum WG Biological Fungicide are considered potential sensitizers, the signal words, “POTENTIAL SENSITIZER”, are required on the principal display panel of all three products.

When handled according to prescribed label instructions, the potential for dermal, eye and inhalation exposure for mixer/loaders, applicators, and handlers exists, with the primary source of exposure to workers being dermal.

In individuals exposed to large quantities of Trianum G Biological Fungicide and Trianum WG Biological Fungicide, respiratory and dermal sensitivity could possibly develop upon repeated exposure to the product since all microorganisms, including *T. harzianum* strain T-22, contain

substances that are potential sensitizers. Therefore, anyone handling or applying Trianum G Biological Fungicide and Trianum WG Biological Fungicide must wear waterproof gloves, long-sleeved shirts, long pants, a dust/mist filtering respirator/mask (NIOSH approval number prefix TC-21) or NIOSH approved respirators (with any N-95, P-95, R-95 or HE filter), and shoes plus socks. In addition, all unprotected workers are restricted from entering enclosed areas (including greenhouses) where Trianum WG Biological Fungicide and Trianum G Biological Fungicide have been handled or applied to soil until dusts have settled.

The health risk to the general population, including infants and children, as a result of bystander exposure and/or chronic dietary exposure is expected to be minimal due the low toxicity/pathogenicity profile for *T. harzianum* strain T-22, Trianum Technical, Trianum G Biological Fungicide and Trianum WG Biological Fungicide, and the absence of sustained increases in exposure to bystanders beyond natural levels. The establishment of an MRL is not required for *T. harzianum* strain T-22.

7.3 Environmental Risk

The non-target organism tests, scientific rationales and supporting published scientific literature submitted in support of Trianum Technical, Trianum G Biological Fungicide and Trianum WG Biological Fungicide were determined to be sufficiently complete to permit a decision on the environmental fate and effects of these products. The use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide containing *T. harzianum* strain T-22 is not expected to pose a risk to non-target organisms when the directions for use on the label are followed.

As a general precaution, the label will also prohibit the direct application of Trianum G Biological Fungicide and Trianum WG Biological Fungicide to aquatic habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs, and wetlands), estuaries or marine habitats, and direct handlers to not contaminate surface water by disposal of equipment wash waters.

No other environmental fate studies or non-target organism studies are required for the proposed use pattern on greenhouse crops, field crops, greenhouse ornamentals and turf.

7.4 Value

The data submitted to register Trianum WG Biological Fungicide and Trianum G Biological Fungicide are adequate to demonstrate efficacy for use on the supported crops in suppressing the proposed pathogens.

Trianum WG Biological Fungicide and Trianum G Biological Fungicide will contribute to Integrated Pest Management (IPM) for many crops by providing a rotational product to growers, ultimately reducing reliance on conventional fungicides. This product will be a valuable tool to organic growers.

T. harzianum is listed as a priority in the Canadian Grower Priority Database (GPD) for the management of cavity spot on carrots. Suppression of this disease is supported on both the Trianum WG Biological Fungicide and Trianum G Biological Fungicide labels. Post-emergence damping off (*Pythium ultimum*) on field lettuce has been identified as a priority in the GPD. Although Trianum WG Biological Fungicide and Trianum G Biological Fungicide have not been identified as a solution for this problem, these products have value as they provide another tool in the management of this disease.

8.0 Proposed Regulatory Decision

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Trianum Technical (containing the active ingredient *T. harzianum* strain T-22), Trianum WG Biological Fungicide and Trianum G Biological Fungicide for the suppression of soil-borne pathogens that cause root diseases on greenhouse crops, field crops, greenhouse ornamentals and turf.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

Human Health

In individuals exposed repeatedly to potentially large quantities of Trianum WG Biological Fungicide and Trianum G Biological Fungicide respiratory and dermal sensitivity may possibly develop. All microorganisms, including *T. harzianum* strain T-22, contain substances that are potential sensitizers. Therefore, anyone handling or applying these products must wear appropriate waterproof gloves, a long-sleeved shirt, long pants, a dust/mist filtering respirator/mask (NIOSH approval number prefix TC-21) or NIOSH approved respirators (with any N-95, P-95, R-95 or HE filter), and shoes plus socks. In enclosed areas including greenhouses, all unprotected workers are restricted from entering areas where Trianum WG Biological Fungicide and Trianum G Biological Fungicide have been handled or applied to soil until dusts have settled.

Environment

The end-use product label will include environmental precaution statements that prevent the contamination of aquatic systems from the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide.

List of Abbreviations

♀	female
♂	male
°C	degree(s) Celsius
ADI	acceptable daily intake
a.i.	active ingredient
ARfD	acute reference dose
bw	bodyweight
CFU	colony forming unit
cm	centimetres
cP	centepoise
DACO	data code
DNA	deoxyribonucleic acid
g	gram
g/m^2	grams per square meter
GH	greenhouse
GPD	Grower Priority Database
h	hour(s)
IPM	Integrated Pest Management
ITS	internally transcribed sequence
kg	kilogram
kg/ha	kilograms per hectare
L	litre
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOC	level of concern
m	metre(s)
MAS	maximum average score
MCC	maximum challenge concentration
mg	milligram
MIS	mean irritation score
mL	millilitre
MPCA	microbial pest control agent
MRL	maximum residue limit
NIOSH	National Institute for Occupational Safety and Health
OECD	Organization for Economic Cooperation and Development
PCR	polymerase chain reaction
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
PubMed	global public domain database on life sciences and biomedical topics which is maintained by the United States National Library of Medicine
RQ	risk quotient
rRNA	ribosomal ribonucleic acid
TSMP	Toxic Substances Management Policy

UK	United Kingdom
UV	ultraviolet
w/w	weight/weight

Appendix I Tables and Figures

Table 1 Toxicity and Infectivity of Trianum Technical and the End Use Products Trianum G Biological Fungicide and Trianum WG Biological Fungicide

Study Type	Species, Strain, and Doses	Results	Comments	Reference(s)
Acute Toxicity/Infectivity of Trianum Technical				
Acute Oral Infectivity and Toxicity (21-Day study)	Rat - Sprague-Dawley 13/sex, single oral dose, ~10^8 CFU/animal, interim sacrifices on Days 1, 3,7,14, and 21 13/sex, untreated, interim sacrifices on Days 1, 3,7,14, and 21 Body weight measured on Days 0 (prior to dosing), 7, 14, and 21	$LD_{50} > 10^8$ CFU/animal	There were no mortalities. One treated female rat demonstrated lethargy, hunched posture and cessation of fecal and urine production beginning on Day 4. This animal appeared normal by Day 7. One male rat in the untreated group had a sore on the neck on Day 17. One treated female lost weight by Day 7, but gained weight by study termination. There were no treatment related lesions at necropsy. Total clearance achieved by Day 2. **LOW TOXICITY, NOT INFECTIVE** **ACCEPTABLE**	PMRA 2337592 and 2337595

Study Type	Species, Strain, and Doses	Results	Comments	Reference(s)
Acute Pulmonary Infectivity and Toxicity (21-Day study)	Rat - Sprague-Dawley 15/sex, ~10^8 CFU/animal in sterile saline, interim sacrifices on Days 1,7, 14, and 21 15/sex, untreated, interim sacrifices Days 1, 7, 14, and 21. Body weight measured on Days 0, 7, 14, and 21.	LD_{50} > 1.65×10^8 CFU/animal	There were no mortalities. All treated animals appeared lethargic following dosing. Animals recovered by Day 1. One treated female and two treated males lost weight between Days 14 and 21. Mottled lungs were observed in 11/15 treated males and females, and enlargement of the lungs were observed in 6/15 treated males and females. MPCA was detected mostly in the lungs, but also in blood, kidney, spleen, and liver treated male and female rats. Clearance was achieved in brain, blood and kidney by Day 7. By Day 21, clearance was achieved in all organs but lungs. A pattern of clearance was observed in lungs by Day 21. **LOW TOXICITY, NOT INFECTIVE** **ACCEPTABLE**	PMRA 2337596

Study Type	Species, Strain, and Doses	Results	Comments	Reference(s)
Acute Intravenous Infectivity (21-Day study)	Rat - CD 15/sex, intravenous injection, ~10^7 CFU/animal, interim sacrifices on Days 1, 7, 14, 21, and 21. 15/sex, untreated, interim sacrifices on Days 1, 7, 14, 21, and 21. Body weights measured on Days 0, 7, 14 and 21	$LD_{50} > 10^7$ CFU/animal	There were no mortalities. One untreated female rat and one untreated male rat lost weight between Days 7 and 14, but gained weight by Day 21. MPCA was detected in brain, lymph nodes, blood, kidney, spleen, liver, and lungs. Clearance was achieved in blood by Day 7 and in brain and lymph nodes by Day 14. By Day 21, Low counts remained in kidney, spleen, liver and lungs. A pattern of clearance was achieved. At necropsy, enlarged spleen in 9/15 treated rats of both sexes. Mottled kidneys were observed in 3/15 treated and untreated females. **LOW TOXICITY, NOT INFECTIVE** **ACCEPTABLE**	PMRA 2337597

Study Type	Species, Strain, and Doses	Results	Comments	Reference(s)
Dermal Irritation	Rabbit-New Zealand white 2♂ 1♀, 4-hour dermal exposure, 0.5 mL Trianum Technical/animal (>2×10^9 CFU/g of *T. harzianum* strain T-22), 2.5×2.5 cm Observed for 72 hours	MIS= 0/8 MAS = 0/8 (24 h, 48 h and 72 h)	No dermal irritation was noted. **NON-IRRITATING** **ACCEPTABLE**	PMRA 2337598
Eye Irritation	Rabbit-New Zealand white 2 ♂; 1 ♀, 24-hour ocular exposure, 0.1mL Trianum Technical/animal (containing >2×10^9 CFU/g), right eye Observed for 72 hours	MIS= 0/110 MAS= 0/110 (24 h, 48 h and 72 h)	No ocular irritation was noted. **NON-IRRITATING** **ACCEPTABLE**	PMRA 2337601
Acute Toxicity and Irritation of Trianum G Biological Fungicide				
Acute Dermal Toxicity	A scientific rationale was submitted by the applicant to waive the requirement for acute dermal toxicity testing based on the nature of the formulation ingredients, the results of acute toxicity/infectivity testing with *T. harzianum* strain T-22, and the results of dermal irritation testing with Trianum G Biological Fungicide. The request to waive testing was accepted.			PMRA 2337756
Dermal Irritation	Rabbit-New Zealand white 1♂ 2♀, 4-hour dermal exposure, 500 mg Trianum G Biological Fungicide/animal (containing 2×10^8 CFU/g of *T. harzianum* strain T-22) in 0.5 mL	MIS= 0/8 MAS= 0/8 (24h, 48 h, and 72 h)	No dermal irritation was noted. **NON-IRRITATING** **ACCEPTABLE**	PMRA 2337757

Study Type	Species, Strain, and Doses	Results	Comments	Reference(s)
	deionized water, 2.5×2.5 cm Observed for 72 hours			
Eye Irritation	Rabbit-New Zealand white 2 ♂; 1 ♀, 24-hour ocular exposure, 100 mg Trianum G Biological Fungicide/animal (containing 2×10^{10} CFU/g of *T. harzianum* strain T-22), right eye Observed for 72 hours	MIS= 3.33/110 (1 h) MAS= 1.78/110 (24 h, 48h, and 72 h)	Conjunctival redness (grades 1–2) was observed in 2/3 eyes after the 1 h timepoint. Redness resolved by 72 hours. Conjunctival chemosis and discharge (grade 1) was observed in 1/3 eyes after 24 hours. Chemosis and discharge resolved by 48 hours. Slight dulling of the cornea was observed in 1/3 eyes after 24 hours. No corneal effects were noted after 48 hours. **MINIMALLY/ SLIGHTLY IRRITATING** **ACCEPTABLE**	PMRA 2337759

Study Type	Species, Strain, and Doses	Results	Comments	Reference(s)
Acute Toxicity and Irritation of Trianum WG Biological Fungicide				
Acute Dermal Toxicity	A scientific rationale was submitted by the applicant to waive the requirement for acute dermal toxicity testing based on the nature of the formulation ingredients, the results of acute toxicity/infectivity testing with *T. harzianum* strain T-22, and the results of dermal irritation testing with Trianum WG Biological Fungicide. The request to waive testing was accepted.			PMRA 2337723
Dermal Irritation	Rabbit-New Zealand white 2♂ 1♀, 4-hour dermal exposure, 0.5 g Trianum WG Biological Fungicide/animal in 0.5 mL deionized water (containing 1.2×10^9 CFU/g *T. harzianum* strain T-22), 2.5×2.5 cm Observed for 72 hours	MIS= 0/8 MAS= 0/8 (24 h, 48, and 72 h)	No dermal irritation was noted. **NON-IRRITATING** **ACCEPTABLE**	PMRA 2337622
Eye Irritation	Rabbit-New Zealand white 1♀ 2♂, 24-hour ocular exposure, 100 mg Trianum WG Biological Fungicide/animal (containing 1.2×10^9 CFU/g *T. harzianum* strain T-22), right eye Observed for 72 hours	MIS= 2/110 (1 h) MAS= 0/110 (24 h, 48 h, and 72 h)	Conjunctival redness (grade 1) was noted after 1 hour in 3/3 eyes. All eye irritation cleared by 24 hours. **MINIMALLY/ SLIGHTLY IRRITATING** **ACCEPTABLE**	PMRA 2337620

Table 2 Toxicity to Non-Target Species

Organism	Exposure	Protocol	Significant Effect, Comments	Reference
Terrestrial Organisms				
Vertebrates				
Birds	Oral – Northern Bobwhite Quail (*Colinus virginianus*), 21 days old	Birds (42) were gavaged with conidia of *T. harzianum* strain T-22 at a dose of 2222 mg/kg bw (9×10^8 CFU/kg bw) for 5 consecutive days. Other groups of birds (14/group) were gavaged with attenuated conidia of *T. harzianum* strain T-22 at a dose of 2222 mg/kg bw, sterile filtrate broth at 1% bw or distilled water at 1% bw for 5 consecutive days and served as attenuated, sterile filtrate and negative controls. Birds were observed for 30 days.	No signs of toxicity or pathogenicity. No mortalities. When compared to controls, there were no apparent effects on body weight or feed consumption. At necropsy, one bird in the treated group was noted with enlarged adrenal glands, but this observation was not considered treatment related as the adrenal glands in the other 41 treated birds appeared normal. 30-day LD50 > 9×10^8 CFU/kg bw (or 2222 mg a.i./kg bw) for 5 consecutive days. **LOW TOXICITY**	PMRA 2337605
	Pulmonary/ Injection	A scientific rationale was submitted to waive testing based on the results of the avian oral study, the biological properties of the MPCA (for example, does not grow ≥37ºC), the lack of adverse effects to birds in published scientific literature and the anticipated low levels of exposure with the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide. No further data are required to assess the risk of harm to birds.		PMRA 2337606
Wild Mammals	A scientific rationale was submitted to waive testing based on the results of the human health and safety testing, the biological properties of the MPCA (for example, does not grow ≥37ºC), the lack of adverse effects to mammals in published scientific literature and the anticipated low levels of exposure with the use of Trianum			PMRA 2337606

Organism	Exposure	Protocol	Significant Effect, Comments	Reference
	G Biological Fungicide and Trianum WG Biological Fungicide. Based on human health and safety testing, it was determined that Trianum Technical was not toxic or pathogenic to mammals via the oral, pulmonary, and intravenous routes. No further data are required to assess the risk of harm to wild mammals.			
Invertebrates				
Arthropods				
Terrestrial Arthropods	Dietary – Bumblebee (*Bombis terrestris*), adult worker	Test 1: Lethal Effects and Sublethal Effects on Reproduction: Bees (5) were placed in artificial plastic nest boxes (15 × 15 × 10 cm). Four artificial nests per treatment, replicated twice. Dietary toxicity: bees were exposed to Trianum WG Biological Fungicide at 0.06%w/v in sugar water or pollen that was sprayed with a 0.06% w/v suspension until saturation. Contact Toxicity: Each bee was topically treated with 50 µL of 0.06% w/v Trianum WG Biological Fungicide Worker survival was evaluated daily for the first 3 days post-treatment, and then on a weekly basis for a period of 11 weeks	No lethal effects on the survival of worker bumblebees or sublethal effects on reproduction were observed. **LOW TOXICITY**	PMRA 2337609

Organism	Exposure	Protocol	Significant Effect, Comments	Reference
		Test 2: Sublethal Effects on Foraging Behaviour Bees (5) were placed in two artificial nest boxes (A and B) connected by a tube of ~20 cm length and 2 cm diameter. In one box (A), the workers constructed their nest. After 2 weeks, food was removed from box A and placed in box B. Before exposure to test material, the workers were allowed a training period of 2 days to forage for untreated food in box B. Afterwards, the sugar water in box B was replaced with sugar water containing 0.06% w/v Trianum WG Biological Fungicide. Four replicates were performed for each treatment, and each experiment was repeated twice. Other groups were similarly treated with tap water and 2 µg a.i./L imidacloprid (previously shown to induce a loss of foraging behaviour in bumblebees) in tap water were included as negative and positive controls for foraging	Trianum WG Biological Fungicide did not cause larval mortality (16.8±4.5 [standard error]) or exert detrimental effects on the production of drones (31.2±1.2 [standard error]). In water control, larval mortality was 10.9±0.4 (standard error) and the production of drones was 28.4±2.9 (standard error). In imidacloprid control, larval mortality was 0.0±0.0 (standard error) and the production of drones was 5.6±0.1 (standard error). **LOW TOXICITY**	

Organism	Exposure	Protocol	Significant Effect, Comments	Reference
		behaviours. Worker survival and drone production were scored on a weekly basis, in a similar manner to that described above, over a period of 9 weeks.		
	A scientific rationale was submitted to waive testing based on the biological properties of the MPCA (for example, not an entomopathogen), the lack of adverse effects to arthropods in published scientific literature and the anticipated low levels of exposure with the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide. No further data are required to assess the risk of harm to terrestrial arthropods.			PMRA 2337606
Non-arthropods				
Terrestrial Non-Arthropod Invertebrates	No information was submitted to address the potential harm to terrestrial non-arthropod invertebrates. Testing is only required for MPCAs that are intended to control non-arthropod invertebrates.			
Plants				
Plants	A scientific rationale was submitted to waive testing based on the biological properties of the MPCA (for example, not a plant pathogen), the lack of adverse effects to plants in published scientific literature and the anticipated low levels of exposure with the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide. Literature searches have only yielded a single report that concluded that the culture filtrate of an isolate of *T. harzianum* reduced various parameters of root and shoot growth in wheat seedlings. These searches have also found numerous reports of beneficial effects through the induction of systemic resistance in various plants following colonization of the plant rhizosphere. No further data are required to assess the risk of harm to terrestrial plants.			PMRA 2337606
Microorganisms				
Micro-organisms	A request to waive the requirement for test data was not submitted. The MPCA is a fungal pathogen which could adversely affect non-target microorganisms. Green mould disease, which was originally assigned to strains of *T. harzianum* is now known to occur only in the related species *T. aggressivum*. The MPCA is a normal component of the soil that is not expected to affect environmentally or economically important microbial species. No further data are required to assess the risk of harm to microorganisms.			

Organism	Exposure	Protocol	Significant Effect, Comments	Reference
Aquatic Organisms				
Vertebrates				
Fish	A scientific rationale was submitted to waive testing based on the biological properties of the MPCA (for example, not a fish pathogen), the lack of adverse effects to fish in published scientific literature and the anticipated low levels of exposure with the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide. There are few reports of recovery of *Trichoderma* from aquatic environments unless the water was polluted. No further data are required to assess the risk of harm to fish.			PMRA 2337606
Invertebrates				
Aquatic Arthropods	A scientific rationale was submitted to waive testing based on the biological properties of the MPCA (for example, not an entomopathogen), the lack of adverse effects to arthropods in published scientific literature and the anticipated low levels of exposure with the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide. There are few reports of recovery of *Trichoderma* from aquatic environments unless the water was polluted. No further data are required to assess the risk of harm to fish.			PMRA 2337606
Aquatic Non-Arthropod Invertebrates	No information was submitted to address the potential harm to aquatic non-arthropod invertebrates. Testing is only required for MPCAs that are intended to control non-arthropod invertebrates.			
Plants				
Aquatic Plants	A scientific rationale was submitted to waive testing based on the biological properties of the MPCA (for example, not a plant pathogen), the lack of adverse effects to plants in published scientific literature and the anticipated low levels of exposure with the use of Trianum G Biological Fungicide and Trianum WG Biological Fungicide. Literature searches have only yielded a single report that concluded that the culture filtrate of an isolate of *T. harzianum* reduced various parameters of root and shoot growth in wheat seedlings. These searches have also found numerous reports of beneficial effects through the induction of systemic resistance in various plants following colonization of the plant rhizosphere. Furthermore, There are few reports of recovery of *Trichoderma* from aquatic environments unless the water was polluted. No further data are required to assess the risk of harm to terrestrial plants.			PMRA 2337606

Table 3 Registered Alternatives (as of March 2014)

Crop	Disease	Active ingredient	Product(s) Name and Reg. No.	Product Type	Resistance Group No.
greenhouse lettuce	bottom rot (*Rhizoctonia solani*)	*Bacillus subtilis*	Taegro	non-conventional	NC*
greenhouse tomato	fusarium	*Streptomyces*	Mycostop Biofungicide	non-conventional	NC
	root diseases (F*usarium*)	*T. harzianum*	Rootshield HC, Rootshield WP, Bora HC, Bora WP	non-conventional	NC
greenhouse cucumber	pythium	*Streptomyces*	Mycostop Biofungicide	non-conventional	NC
	Pythium spp.	metalaxyl	Ridomil Gold 480SL	conventional	4
	pythium damping off (*Pythium* spp.)	cyazofamid	Cyazofamid 400 SC, Torrent, Ranman 400SC	conventional	21
	post-emergence damping off (*Pythium* spp.)	*Streptomyces lydicus*	Actinovate SP	non-conventional	NC
	pre-emergence damping off (*pythium* spp.)	garlic powder	Influence WP	non-conventional	NC
	root diseases (*pythium*)	*T. harzianum*	Rootshield WP, Bora HC, Bora HP	non-conventional	NC
	root rot (*Pythium* spp.)	*Streptomyces lydicus*	Actinovate SP	non-conventional	NC
		garlic powder	Influence WP	non-conventional	NC
		cyazofamid	Cyazofamid 400 SC, Torrent 400SC, Ranman 400SC	conventional	21
greenhouse ornamental	pythium	*Streptomyces*	Mycostop Biofungicide	non-conventional	NC
	pythium	fosetyl AL	Chipco Aliette Ornamental,	conventional	U

Crop	Disease	Active ingredient	Product(s) Name and Reg. No.	Product Type	Resistance Group No.
	pre-emergence damping off (*pythium* spp.)	garlic powder	Influence WP	non-conventional	NC
	root diseases (*pythium*)	*T. harzianum*	Rootshield WP, Rootshield HC, Bora HC, Bora HP	non-conventional	NC
	root rot (*Pythium* spp.)	garlic powder	Influence WP	non-conventional	NC
greenhouse ornamentals	fusarium	*Streptomyces*	Mycostop Biofungicide	non-conventional	NC
	root diseases (F*usarium*)	*T. harzianum*	Rootshield HC, Rootshield WP, Bora HC, Bora WP	non-conventional	NC
	fusarium wilt (*Fusarium oxysporum*)	*Trichoderma asperellum*	T34 Biocontrol	non-conventional	NC
field lettuce	damping off (*R. solani*)	*Gliocladium catenulatum*	Prestop	non-conventional	NC
	pre-emergence damping off (*R. solani*)	azoxystrobin	Dynasty 100SF	conventional	11
	rhizoctonia damping off (*R. solani*)	*Bacillus subtilis*	Serenade Soil	non-conventional	NC
	rhizoctonia root rot (*R. solani*)	*Bacillus subtilis*	Serenade Soil	non-conventional	NC
	bottom rot (*R. solani*)	*Bacillus subtilis*	Taegro	non-conventional	NC
field carrots	*Pythium* spp.	chloropicrin	Chloropicrin 100 Liquid Soil Fumigant	conventional	multi-site
	soil borne diseases (*Pythium* spp.)	chloropicrin	Pic Plus Fumigant	conventional	multi-site
	cavity spot	cyazofamid	Torrent 400SC	conventional	21
	cavity spot (*Pythium* spp.)	cyazofamid	Cyazofamid 400 SC, Ranman 400SC	conventional	21
		metalaxyl	Ridomil Gold 480SL	conventional	4

Crop	Disease	Active ingredient	Product(s) Name and Reg. No.	Product Type	Resistance Group No.
		fenamidone	Reason 500SC	conventional	11
		Bacillus subtilis	Serenade Soil	non-conventional	NC
	damping off (*Pythium*)	fenamidone	Reason 500SC	conventional	11
		metalaxyl	Apron XL LS	conventional	4
	pythium root rot (*Pythium* spp.)	*Bacillus subtilis*	Serenade Soil	non-conventional	NC
Turf	dollar spot	chlorothalonil	Daconil 2787 Flowable, Daconil 720, Daconil Ultrex	conventional	M
		thiophanate-methyl	Proturf Granular	conventional	1
		propiconazole	Banner 130 EC, Banner Maxx	conventional	3
		myclobutanil	Eagle, Golden Eagle	conventional	3
	dollar spot (*Sclerotinia homoeocarpa*)	thiophanate-methyl	Senator 70WP 1, Senator 70WP, Senator 70 WP WSB1	conventional	1
		iprodione	Rovral, Rovral WDG, Proturf Granular X, Green GT, Quali-Pro Iprodione 240 SE, Iprodione Turf and Ornamental	conventional	2
		propiconazole	Quali-Pro Propiconazole 14.3 ME, The Andersons 0.72% Prophesy on DGPro	conventional	3

Crop	Disease	Active ingredient	Product(s) Name and Reg. No.	Product Type	Resistance Group No.
		boscalid	Cadence WDG	conventional	7
		penthiopyrad	Velista	conventional	7
		pyraclostrobin	Insignia EG	conventional	11
		fluoxastrobin	Disarm 480 SC	conventional	11
		propiconazole, azoxystrobin	Headway	conventional	3, 11
		propiconazole, chlorothalonil	Concert	conventional	3, M
		Bacillus subtilis	Rhapsody ASO	non-conventional	NC
		mineral oil	Civitas	non-conventional	NC
	microdochium patch or fusarium patch (*Microdochium nivale*)	iprodione	Green GT, Quali-Pro Iprodione 240 SE	conventional	2
		propiconazole	Quali-Pro Propiconazole 14.3 ME	conventional	3
		azoxystrobin	Heritage, Heritage Maxx	conventional	11
		trifloxystrobin	Compass 50WG	conventional	11
		pyraclostrobin	Insignia EG	conventional	11
		propiconazole, azoxystrobin	Headway	conventional	3, 11
		propiconazole, chlorothalonil	Concert	conventional	3, M
	pink snow mold (*Microdochium nivale* or *Fusarium nivale*)	chlorothalonil	Daconil 2787 Flowable, Daconil 720,	conventional	M
		iprodione	Green GT, Quali-Pro Iprodione 240 SE, Rovral, Rovral WDG, Proturf Granular Fungicide X	conventional	2

Crop	Disease	Active ingredient	Product(s) Name and Reg. No.	Product Type	Resistance Group No.
		propiconazole	Quali-Pro Propiconazole 14.3 ME, Banner 130 EC, Banner Maxx	conventional	3
		azoxystrobin	Heritage, Heritage Maxx	conventional	11
		trifloxystrobin	Compass 50WG	conventional	11
		pyraclostrobin	Insignia EG	conventional	11
		propiconazole, azoxystrobin	Headway	conventional	3, 11
		fluoxastrobin	Disarm 480 SC	conventional	11
		mineral oil	Civitas	non-conventional	NC

*: not classified

Table 4 List of Supported Uses

Proposed Use Claim	Supported Use Claim
Suppression of *Rhizoctonia solani* (bottom rot, collar rot, root rot, damping off, wire stem) on greenhouse lettuce at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants	Supported as suppression of post-emergence damping off (*Rhizoctonia solani*) on greenhouse lettuce at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants
Suppression of *Fusarium oxysporum* (fusarium wilt, tomato wilt, fusarium root rot, fusarium crown rot) on greenhouse tomatoes at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants	Supported as suppression of fusarium root rot and fusarium crown rot (*Fusarium oxysporum*) on greenhouse tomatoes at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants
Suppression of *Pythium ultimum* (pythium root rot, pythium water mold, damping off) on greenhouse cucumbers at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants	Supported as suppression of post-emergence damping off (*Pythium ultimum*) on greenhouse cucumbers at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants

Proposed Use Claim	Supported Use Claim
Suppression of *Pythium ultimum* (pythium root rot, pythium water mold, damping off) on greenhouse ornamentals (pansy, chrysanthemum, saintpaulia) at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants	Supported as suppression of post-emergence damping off (*Pythium ultimum*) on greenhouse ornamentals at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants
Suppression of *Fusarium oxysporum* (fusarium wilt, fusarium root rot, fusarium crown rot) on greenhouse ornamentals (pansy, chrysanthemum, saintpaulia) at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants	Supported as suppression of fusarium root rot and crown rot (*Fusarium oxysporum*) on greenhouse ornamentals at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants
Suppression of *Rhizoctonia solani* (bottom rot, collar rot, root rot, damping off, wire stem) on field lettuce at a rate of: (i) 1.5 g/m^2 at sowing (ii) 3 kg/ha at planting	Supported as suppression of post-emergence damping off (*Rhizoctonia solani*) on field lettuce at a rate of: (i) 1.5 g/m^2 at propagation (ii) 1.5-3.0 g/m^2 at planting or 15-30 g/1000 plants
Suppression of *Pythium violae* (cavity spot) on field carrots at a rate of: (i) 1.5 kg/ha in furrows (ii) 2.5 kg/ha in beds	Supported as suppression of cavity spot (*Pythium violae*) on field carrots at a rate of: (i) 1.5 kg/ha in furrows (ii) 2.5 kg/ha in beds
Suppression of *Sclerotinia homoeocarpa* (dollar spot) on turf at a rate of: (i) 1st and 2nd application: 30 g/100 m^2 (ii) Subsequent appl. on fairways/tees: 15 g/100 m^2 (iii) Subsequent appl. on greens: 30 g/100 m^2	Supported as <u>reduces symptoms of</u> dollar spot (*Sclerotinia homoeocarpa*) on turf at a rate of: (i) 1st and 2nd application: 30 g/100 m^2 (ii) Subsequent appl. on fairways/tees/greens: 15 g/100 m^2
Suppression of microdochium patch, pink snow mold (Microdochium nivale) on turf at a rate of: (i) 1st and 2nd application: 30 g/100 m2 (ii) Subsequent appl. on fairways/tees: 15 g/100 m^2 (iii) Subsequent appl. on greens: 30 g/100 m^2	Supported as <u>reduces symptoms of microdochium</u> patch (*Microdochium nivale*) on turf at a rate of: (i) 1st and 2nd application: 30 g/100 m^2 (ii) Subsequent appl. on fairways/tees/greens: 15 g/100 m^2
Application method: drench, through drip-irrigation systems, or by spray at sowing.	Application method: drench or by spray at sowing.

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A. List of Studies/Information Submitted by Registrant

1.0 The Active Substance, Its Properties and Uses

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2.0 Human and Animal Health

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2337598 2012, Trianum Technical Acute Dermal Irritation in Rabbits, DACO: M4.5.2
2337600 2012, Tier 1: Microbial Pesticide Studies Reporting of Hypersensitivity Incidence, DACO: M4.6
2337601 2012, Trianum Technical Acute Eye Irritation in Rabbits, DACO: M4.9
2337620 2012, Trianum WG (Water Dispersible Granule) Acute Eye Irritation in Rabbits, DACO: M4.9
2337621 2012, Tier 1 Microbial Pesticide Studies Reporting of Hypersensitivity Incidence, DACO: M4.6
2337622 2012, Trianum WG (Water Dispersible Granule) Acute Dermal Irritation in Rabbits, DACO: M4.5.2
2337623 2012, Tier 1: Microbial Pesticide Mammalian Toxicology Data Requirements Satisfaction of Data Requirements with Literature/Rationale and Data Waivers, DACO: M4.4, M4.9
2337624 2013, Trianum WG Biological Fungicide *Trichoderma harzianum* Rifai Strain KRL AG-2 (also called T-22) - A Condensed Comprehensive Data Summary (Part M4), DACO: M4.2.2, M4.2.3, M4.3.2, M4.3.3, M4.4, M4.5.2, M4.6, M4.9
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2337754 2013, Trianum G Biological Fungicide *Trichoderma harzianum* Rifai Strain KRL AG-2 (also called T-22) - A Condensed Comprehensive Data Summary (Part M4), DACO: M4.2.2, M4.2.3, M4.3.2, M4.3.3, M4.4, M4.5.2, M4.6, M4.9
2337756 2012, Tier 1: Microbial Pesticide Mammalian Toxicology Data Requirements Satisfaction of Data Requirements with Literature/Rationale and Data Waivers, DACO: M4.4, M4.9
2337757 2012, Trianum G (Granule) Acute Dermal Irritation in Rabbits, DACO: M4.5.2

2337758 2012, Tier 1 Microbial Pesticide Studies Reporting of Hypersensitivity Incidence, DACO: M4.6
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3.0 Environment

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2337606 2012, Tier 1: Microbial Pesticide Non-Target Organisms and Environmental Fate Data Satisfaction of Data Requirements with Literature/Rationale, DACO: M9.2.1, M9.2.2, M9.3, M9.4.1, M9.4.2, M9.5.1, M9.5.2, M9.8.1
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2337618 2013, Trianum WG Biological Fungicide *Trichoderma harzianum* Rifai Strain KRL AG-2 (also called T-22) - A Condensed Comprehensive Data Summary (Part M9), DACO: M9.2.1, M9.2.2, M9.3, M9.4.1, M9.4.2, M9.5.1, M9.5.2, M9.8.1, M9.8.2, M9.9
2337762 2013, Trianum G Biological Fungicide *Trichoderma harzianum* Rifai Strain KRL AG-2 (also called T-22) - A Condensed Comprehensive Data Summary (Part M9), DACO: M9.2.1, M9.2.2, M9.3, M9.4.1, M9.4.2, M9.5.1, M9.5.2, M9.8.1, M9.8.2, M9.9
2337763 2012, Tier 1: Microbial Pesticide Non-Target Organisms and Environmental Fate Data Satisfaction of Data Requirements with Literature/Rationale, DACO: M9.2.1, M9.2.2, M9.3, M9.4.1, M9.4.2, M9.5.1, M9.5.2, M9.8.1, M9.8.2

4.0 Value

2337634 2011, Final Report: To determine the efficacy of Trianum-P and Trianum-G applied preventatively and Enzicur applied curatively on microdochium patch in fine amenity turf, DACO: M10.2.2,M10.3.2.1

2337635 2010, Final Report: To determine the efficacy of Trianum-P and Trianum-G applied preventatively and Enzicur applied curatively on dollar spot in fine amenity turf, DACO: M10.2.2,M10.3.2.1

2337637 2010, Define efficacy of Trianum for control of rhizoctonia in lettuce, DACO: M10.2.2

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2337650 2011, Assessment of the efficacy of Trianum WG on *Fusarium oxysporum* f.sp. *radicis- lycopersici* in tomato, DACO: M10.2.2

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2337659 2011, Assessment of the efficacy of different formulations of Trianum on *Fusarium oxysporum* f.sp. *radicis-lycopersici* in tomato, DACO: M10.2.2

2337660 2010, Assessment the efficacy of KBP11 and KBG11 biocontrol products against *Fusarium oxysporum* f. sp. *radicis lycopersici* in tomato crop, DACO: M10.2.2

2337661 2010, Assessment the efficacy of TRIANUM biocontrol product against *Fusarium oxysporum* f. sp. *radicis lycopersici* in tomato, DACO: M10.2.2

2337727 2012, Evaluation of Crop safety and Efficacy of Trianum-G and Trianum-P used in Chrysanthemum, DACO: M10.2.2

2385523 2012, Cavity spot in carrots, DACO: M10.2.2,M10.3.1

2385530 2012, Control of cavity spot and sclerotinia in carrots using Trianum 2011, DACO: M10.2.2, M10.3.1

2385534 2011, To determine the efficacy of Trianum on Dollar spot affecting managed amenity turf, DACO: M10.2.2,M10.3.1

2385535 2011, Turf Trail Trianum dollarspot France, DACO: M10.2.2,M10.3.1

B. Additional Information Considered

i) Published Information

1.0 Chemistry

2.0 Human and Animal Health

3.0 Environment

4.0 Value

ii) Unpublished Information

1.0 Chemistry

2.0 Human and Animal Health

3.0 Environment

4.0 Value